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DAVID JOHN THOMAS, F.R.C.S., A FOUNDER OF VICTORIAN MEDICINE.[1]

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DAVID JOHN THOMAS represents the type of young man who built the foundations of our society in Victoria. The first settlers in this most distant corner of the Empire were nearly all young men and adventurers, who chose pioneering instead of the security of life at home. The period between 1839 and 1871 covers the establishment of European settlement in Victoria; a period during which such men as Morton and Simpson, Bright and Addison, Pasteur and Lister, were changing the face of medicine. It is against this background that we must regard the practice of medicine in this isolated colony. Here we do not expect to find work of genius and discovery, but the work of young men battling against nature and isolation to establish the settlement. Let us glimpse into the past and appraise the efforts of one of their leaders.

[1] Read at a meeting of the Section of Medical History of the Victorian Branch of the British Medical Association, September 5, 1955.

Youth and Education.

Thomas was born on September 12, 1813, to Ann, wife of William Thomas, gentleman, of Llwyn-y-berllan, Caermarthenshire, South Wales. Little is known of his childhood up to the commencement of his medical education. His mother died when he was only fourteen years old, and his father married again. David was the eldest son of four boys and three girls, and inherited the family estate at an early age. One brother, Charles, and two sisters, Mary Anne and Sarah, eventually followed him to Victoria. He was quite young when he sold the property to Sir Robert Peel's brother, and with the proceeds Thomas supported the other members of the family and educated himself. During these years he showed a propensity for easy spending, and the family money soon disappeared.

We have no intimation why this country youth desired to study medicine, but he began as an apprentice in the Swansea Infirmary in 1834 (Thomas, 1860). His "good conduct and assiduous attention to his duties" received the acclaim of his teachers, the chief one of whom was George C. Bird, senior surgeon. Bird was obviously impressed and had a great personal liking for Thomas, whose professional abilities he considered were "of very superior order". There was "no young man in whom he should have greater confidence".

In 1836, after acquiring "a good preliminary and practical knowledge of his profession", Thomas went to London, where he studied surgery under Robert Liston and Samuel Cooper at University College Hospital. His teacher in medicine was Anthony T. Thomson. Cooper had "no doubt that he [would] prove an efficient and honourable member of the profession". During these student days he lived highly and showed a youthful vitality which characterized his later life and surgery in Port Phillip. He graduated with the Licentiate of the Society of Apothecaries and the Membership of the Royal College of Surgeons early in 1838, and took a position as house surgeon at the Royal Lying-In Hospital, Queen Street, Golden Square.

Thomas planned to become a visiting assistant after leaving the hospital, in order to prepare himself for the routine of general practice. However, while waiting in London to take out his degree of doctor of medicine, he met Mr. Buckley an old school-fellow and master of a small vessel, the *Louisa Campbell*. This meeting changed Thomas's life. The *Louisa Campbell* was preparing to sail for Van Diemen's Land, and one imagines that Buckley had little difficulty in persuading the adventurous-spirited young Thomas to sail with her as ship's surgeon for the round trip.

Arrival in Port Phillip.

The *Louisa Campbell* left London in 1838, and after an apparently uneventful voyage arrived in Launceston early in 1839. On the way home she called at the new settlement of Port Phillip to pick up the first cargo of wool to leave Victoria. Thus Thomas arrived at Melbourne in January, 1839 (Graham, 1952). We may well wonder what were Thomas's impressions of the bustling town of scarcely 2000 inhabitants "protected by ten constables and a chief, twenty-five soldiers for guard and escort duty, and two hundred and fifty ticket of leave men" (McCrae, 1934). His spirit must have been somewhat dampened by the mode of his disembarkation. Thomas, who had a slight impediment in his speech, often related the story, "stuttering delightfully as he always did" (Finn, 1888). On leaving the ship the boat was swamped, and, after swimming ashore, he tramped about six miles at dead of night through the bush to Robert Russell's cottage on the Yarra bank. On his arrival "the watchdog seized him, and on hearing his cries [Russell], in no good humour, called out to him to take the boat which he did and went flying down the Falls in the dark, bringing up opposite Fawkner's Pub, where no doubt his troubles ended" (Finn, 1888). "Garryowen" (Edmund Finn, 1819-1898) also states that Thomas was "in some measure addicted to stimulants"—perhaps this episode confirmed his addiction.

However, Port Phillip did impress Thomas, for he was soon persuaded by solicitations of several prominent citizens, particularly C. H. Ebden, of Black Rock House, to stay and practise in the new colony. The doctors already practising in the colony at that time were Barry Cotter, Patrick Cussen, David Patrick, McCurdy and probably John Sproat. Thomas first lived in Queen Street, but soon moved to the north side of Bourke Street West, where he overlooked the old St. James's Cathedral. The *Louisa Campbell* returned without a ship's surgeon.

The Early Victorian Period.

His practice soon throve, for Thomas, with his Puckish sense of humour, became a popular young man. Later in 1839 the arrival of the *Midlothian* from Leith was an event of immense importance to him. She brought Dr. Farquhar McCrae with his mother and wife and sisters. McCrae immediately joined Thomas in partnership, and on December 1, 1840, Thomas married Farquhar's sister, Margaret Forbes McCrae. The young couple quickly settled into the early Victorian social life of the town. *Georgiana's Journal* for 1841 (McCrae, 1934) often refers to them.

> Mrs. Thomas, not approving of Mrs. M. (tho' of good yeoman ancestry) stayed away.
>
> Farquhar suffering from an eruption on his face—Dr. T. tells me it is called "Dibble dibble"—a kind of confluent pock—much more offensive even than smallpox.
>
> Mrs. Thomas and Mary Anne came to look at our garden, surprised at the progress it had made.
>
> Dr. Thomas tells me I have "low fever" or "Swamp fever" which is just now raging at back of Brighton.

With the general recession of 1840 Thomas suffered some financial embarrassment, but he had already taken responsibility for his two sisters, who arrived in March that year in *The Eagle*, with the same Captain Buckley. His brother Charles was already in Melbourne preparing for pastoral pursuits, and was a constant drain on Thomas's purse.

Medical practice was arduous in the forties, and good horsemanship was a necessity. Thomas writes (1865*f*) of this period as follows:

> Indeed, I almost lived on horse-back, and I was at all times prepared to start to attend any patient under 80 miles; this I would do and return in about 16 hours. Of course I had several relays. This distance was not at all uncommon, and I continued at this sort of work for 10 years, when, in 1849, the town had so increased in dimensions and population that I limited my practice to Melbourne and the suburbs. So you can imagine that I had little time to study.

Thomas often drove with Wilkie, Cussen and Black for week-ends at Queenscliff, where the Reverend James Clow, Wilkie's father-in-law, lived on the beautiful old "Oakhill" property. His four-in-hand would be seen regularly at Flemington Racecourse. Thomas's popularity is reflected in his being the obvious choice when a surgeon was required at Melbourne's first duel. "Garryowen" tells us of the hotel argument between Thomas Rymie and Peter Snodgrass, during which the challenge was given and accepted. The young men chose Thomas, "a surgeon of considerable skill, and an ardent lover of practical jokes", for their surgeon, and he accepted the position "without much reluctance". However, this time the joke turned on him. One contestant pulled the trigger prematurely and the ball abraded his big toe. In their disappointment the spectators grasped Thomas's new bell-topper for their target—against stuttered and vehement objections from its owner. The hat was soon ruined, and Melbourne's "gay blades" returned for well-earned rest after the night's entertainment (Finn, 1888).

Thomas was usually the joker. One evening, after he had wined and dined very adequately, he staggered up to a cabby. The following dialogue ensued:

> Doctor T.: I say, my good fellow, do you know Dr. Thomas?
>
> Cabby: No Sir.
>
> Doctor T.: Well then, do you know Dr. Wilkie?
>
> Cabby: No Sir.
>
> Doctor T.: What, do you really mean to say you do not know either of these fellows? By Jove, you must be a new chum.
>
> Cabby: Just so your Honour. I only landed in Melbourne last week.
>
> Doctor T.: Well, then, look you here. I am Dr. Wilkie, and I have "grogged" so much that, as you see, I am hardly able to stand. In this condition I am not game to face home tonight, so I shall sleep at Dr. Thomas's, and I want you to drive me to his house in Bourke Street. At 2 o'clock tomorrow you will call at Dr. Wilkie's in Swanston Street, when I will pay you double fares.
>
> Cabby: Aye, aye Sir. Let me help you into the trap.

Wilkie was a pillar of the Presbyterian Church, and "his indignation was intense at the shameful unprofessional manner in which he had been impersonated" (Finn, 1888). However, the cabby was paid. Thomas often made Wilkie the butt of his jokes, and this later led to a very strained relationship between them.

Another of his jokes led to his friend the editor of *The Argus* being met at his office one morning by a full funeral cortege. The undertaker had received notice of

the editor's sudden death the night before and of his intended early burial. The corpse proved very much alive, and again Thomas paid the bill (Finn, 1888).

Early Surgery.

The first facilities for hospital treatment were established in 1841, when Wilkie, Myers, O'Mullane and Thomas formed the staff of a stop-gap hospital of 20 beds in a two-story building in Bourke Street West, probably made available by John Fawkner. In these "most inadequate and inconvenient" quarters their surgery was performed. Amputations were their commonest operations, and the incidence of "hospital infection" was high (Graham, 1948). Thomas later claimed to be the first surgeon in the Colony to ligate the radial, femoral (1846), carotid and external iliac arteries, to excise the upper jaw, and to perform Syme's amputation and Syme's perineal section, "as well as many other amputations and operations" (Thomas, 1865*b*).

One case he reports is of considerable interest, for it was, I believe, the first time a laparotomy was performed in Australasia. In 1846 Thomas was called to see a Mr. Clarke, who was "emaciated, weak and of cachectic aspect with a tumour in the right side of the abdomen. This was causing excruciating pain, and Thomas considered it to be in the intestines. He reported as follows (Thomas, 1864*d*):

> The only alternative to leaving it alone was to cut it out. In the presence of Sir James Palmer, Mr. Griffin and others I opened the abdominal parietes on the right side over the tumour. When the colon was exposed, the lump was found to be within the gut, but, unfortunately, the intestine was in a hard scirrhous state down to the caecum. Further procedure was therefore deemed useless, the cut edges were brought together and united by twisted sutures. He died a few weeks afterwards, the parts having previously united.

The Port Phillip Medical Association.

The story of the formation of the Port Phillip Medical Association, the first meeting of which was held in the Prince of Wales Hotel in 1846, has already been told in detail (Graham, 1952). It suffices to say that Thomas played a leading part from its inception and was one of its first committeemen. However, it is interesting to note that in later reminiscences he tells of earlier, though unofficial, medical meetings long before this association was founded (Thomas, 1862*a*):

> In my early career in this Colony, we had no medical periodical, and our former medical meetings, *commencing in* 1840 partook more of the character of a conversation than a regularly organized scientific association. We used to have capital dinners, and first rate social and intellectual evenings. Old time and bad times, conventionality and advanced civilization have sobered us all. I would not from these remarks, lead you to suppose that we, in the slightest degree, exceeded the bounds of propriety, but that we conformed with the habits of the day in combining business with pleasure, jollity with gravity, intellectuality with frivolity. Nevertheless we had most instructive professional discussions, and I have no hesitation in stating that the professional standard then would bear comparison with that as it at present exists.

The Port Phillip Medical Association foundered on the rock of petty internal bickering, in which Thomas had his share. When reading of its history one forms the impression that he was always striving for peace among the members and was usually very fair in his criticism, although he had the ability to say exactly what he thought.

Anæsthesia.

In October, 1846, just after the Port Phillip Medical Association was formed, Morton gave his historic demonstration of the use of ether. News travelled slowly then, and it was not until December that Liston, in London, first operated upon an anæsthetized patient. The history of the introduction of anæsthesia into Australia has been written (Howard, 1933; Potter, 1938; Crowther, 1947; Gandevia, E., 1954). William Pugh, of Launceston, first used ether on June 7, 1847, and it was given in Sydney shortly afterwards. Port Phillip was the youngest Colony and was usually late in receiving news from abroad. It is therefore not surprising to find that Thomas was about a month behind the others. He had practised on himself with ether before using it first on a patient on August 2, 1847. The instrument he used was copied from Mr. Robinson's, as shown in the *London Illustrated News*, and consisted of a pipe which was placed in the mouth with the nostrils clipped closed. Air was drawn over ether-soaked sponges in two flasks and through this narrow airway.

FIGURE I.
David John Thomas, from a daguerreotype, *circa* 1850.

There was intense public interest in this momentous event. *The Port Phillip Patriot*, a local daily, broadcast the news to the Colony on August 3, 1847:

> Painless Surgery.—Dr. Thomas has been the first surgeon in this Province who has adopted and with signal success, the process of "painless surgery" as lately practised in the mother country. Yesterday, assisted by Doctors Playne and Campbell he amputated the arm of a patient under the influence of either,[1] and the time occupied in procuring, by inhalation, the necessary insensibility, was two minutes and the operation was performed in forty seconds.

(Another newspaper report described this as "an unusually short space of time".)

It is interesting to compare the surgery and conditions in the Colony with our present state. The patient, Mr. Egan, aged fifty-three years, was duck-shooting in the country beyond the Campaspe River when the fowling piece of his gun burst. The injury to his left arm "extended from three inches above the wrist on the anterior aspect, as far as the metacarpo-phalangeal articulation. The whole wrist and palm were laid bare . . . the flexor tendons together with the aponeurosis and fascia on the palmar aspect of the wrist joint was completely torn asunder, and the thumb . . . was dangling by a piece of ligament by which alone it was attached to the hand" (Thomas, 1847). The hæmorrhage was stemmed by a neighbour.

[1] *The Port Phillip Patriot* corrected this spelling error next day.

He visited two doctors in a spring cart, only to find them away, and then decided to come to Melbourne (a distance of nearly 100 miles) in a chaise cart. The journey, over bush roads in Victorian winter weather, took three days in that uncomfortable vehicle. Little wonder that on his arrival his pulse was weak and rapid, and he was pale and exhausted and subject to frequent fainting attacks. His wound by this time was "in a sloughing state". He had a below-elbow amputation, and four weeks later rode back over the same roads. Such were the conditions in the forties.

Thomas used ether on several occasions shortly after this, and collected his experiences for the Colony's young medical association. At the ordinary monthly meeting of the Port Phillip Medical Association, held at Dr. Wilkie's house on September 7, 1847, he read a paper entitled "On the Inhalation of the Vapour of Æther with Cases". This has erroneously been recorded as the first scientific paper read to a medical society in Victoria (Nield, 1871; Cowen, 1933). The first was given by Dr. Wilkie and the second by Dr. Greeves. This was the third (Graham, 1952). In this paper Thomas showed a better perspective than other pioneers of anæsthesia here. Pugh himself had reason to "regret that further acquaintance with this much lauded agent had tended materially to lessen its value in [his] estimation". He felt its fame would be short-lived (Crowther, 1947). The *Australian Medical Journal* of June and July, 1847, was even more derogatory. Two successive editorials had "no hesitation in predicting for this process a transient popularity; it will have its day, ultimately to be abandoned as useless or injurious".

Thomas was at least the first champion of anæsthesia in Australia. In this critical atmosphere he hailed it as "one of the most felicitous improvements to modern practice". Apart from the relief of pain, it allowed more meticulous dissection with "as much certainty in the living as in the dead". He deemed it "the duty of every member of the profession to come forward to state the results of his experiences", and he decried Pugh's criticism, given without stating the reasons for his loss of confidence. He made a plea to men who observed "injurious effects" to report them. Thomas concluded:

> I look upon it as one of the greatest blessings bestowed on mankind, and . . . I consider that when the mode of its employment is better known its use will become general.

This was the attitude of a man in the most distant corner of the Empire—only ten months after the first introduction of ether. His paper was prepared for publication in the *Australian Medical Journal*, but it was not printed until 1934, for this journal ceased to be only six months after its inception in 1846 (Thomas, 1847; Cowen, 1933).

Thomas later claimed to have introduced chloroform into Victoria; but the earliest case report I can find is in *The Port Phillip Patriot*, August 25, 1848. In this case A. O'Mullane gave the anæsthetic while Dr. Thomas operated "in a scientific manner in the presence of 8 or 10 medical men. The time occupied from the first incision of the knife to the securing of the arteries was scarcely half a minute". He was also the surgeon when Victoria suffered its first anæsthetic death. His partner, Edward Barker, was the anæsthetist. The patient was a man "addicted to intemperance", who had a *fistula-in-ano*. He died after a convulsive seizure, which began after a very small amount of chloroform had been given (*Medical Times and Gazette*, 1852).

The Melbourne Hospital.

In 1847 arrangements were made to staff the new Melbourne Hospital, at that time under construction on the corner of Swanston and Lonsdale Streets. The system of election of the staff by the governors of the hospital was then born. *The Port Phillip Patriot*, July 1, 1847, reports a meeting of the committee of the Hospital at which a motion was passed, stating:

> That all gentlemen declared legally qualified medical practitioners, by either the N.S.W. or Port Phillip Medical Board, shall be eligible as Physicians or as Surgeons in the Hospital.

Below this appear notices of application by several prominent practitioners — A. O'Mullane, Augustus F. A. Greeves, E. C. Hobson, W. H. Campbell, and also D. J. Thomas. The latter reads as follows:

> To the Governors of the Melbourne Hospital.
>
> GENTLEMEN—As the period will shortly arrive for the election of Medical Officers to your valuable institution, I beg to inform you that it is my intention to become a candidate for the office of one of your surgeons.
>
> Should you honour me by electing me, I shall use every exertion in my power to carry out the objects and in every way promote, the interests of the institution. With the highest respect.
>
> I have the honor to be,
> Gentlemen,
> Your Obedient Servant
> D. J. Thomas, M.R.C.S.L.

Thus the advertising began. "Garryowen" (Finn, 1888*d*) reports: "The election . . . was accordingly held on the 15th July, 1847, presided over by the Major (Mr. Moor), and notwithstanding all the money spent on advertising and other ways it was a walkover." Thomas topped the poll and was elected with Greeve and Campbell as the first surgeons to the Melbourne Hospital. He continued to serve on the staff, apart from six years while he was in Europe, until his death in 1871.

Medical Practice.

By 1850 Thomas, now a member of the Port Phillip Medical Board, had "unquestionably the largest practice in the colony", and his financial position seemed assured. In that year, after McCrae's departure to Sydney, he joined Edward Barker in legal partnership (*Australian Medical Journal*, 1856). Barker had just returned to practice after nine years as a pastoralist.

The gold rush only helped to improve their position, for it brought an influx not only of patients, but also of doctors — and charlatans. Many practitioners migrated to the goldfields, and over one tent in Ballarat hung a sign: "Thomas and Barker, Surgeons". There is no evidence that Thomas practised in this tent, but undoubtedly his partner did represent the firm. "Garryowen" tells of the occasion when thieves ransacked the tent and stole £200 while Barker was away on a false call (Finn, 1888).

Thomas visited the goldfields in a three-day sightseeing tour with a large party of Melbourne society which he organized. He drove "the ladies in a four-horse waggon like a brake". Thomas was described by "Garryowen" as being not only a good doctor, but an excellent whip. In the Pentland Hills (Finn, 1888) "they had to ascend a very steep hill . . . . All the ladies had to walk, and at the summit there was a stiff pinch for about 50 yards, with a narrow track only wide enough for one vehicle, and on the other side was a steep precipice of some hundred feet. Dr. Thomas had to get his four horses up this and then turn the leaders before the wheelers to avoid going down the precipice . . . . The ascent of this was the finest piece of driving I have ever witnessed."

European Tour, 1853 to 1859.

We are perhaps surprised to find that in 1853 Thomas decided to tour Europe with his family. He had spent fifteen years in the Colony and had established his supremacy in the profession. The trip was, we suppose, partly to study the latest advances in surgery and partly to renew old family friendships. Before he left he received many tributes.

The governors of the Melbourne Hospital, on his retirement from the staff, passed the following motion (Thomas, 1860).

> That the Governors, in accepting the resignation of David John Thomas Esq., one of the Surgeons of the Melbourne Hospital, desire to express their high sense of the eminent professional ability and skill, as well

as the kindness and attention, shown by him in fulfilling the duties of his office from the opening of the Institution; and, as the only other mark of their approval, it is ordered that the necessary steps be taken for constituting him an Honorary Governor of the Institution.

Thomas also bore a letter of credence from Latrobe, the Lieutenant-Governor. *The Argus* on February 5, 1853, reported that "his departure leaves a blank in the lists of our medical men which will not be readily filled". From his professional brothers he received a "very kind and flattering address [Figure II] . . . and a sum of upward of £60" for Mrs. Thomas to purchase something for her husband in England (Thomas, 1860).

Thomas, with his wife and five daughters, left Melbourne in the *Northumberland*, a ship of 812 tons carrying 33 "statute adults", on Febrary 3, 1853. A fellow passenger was Sir William a'Beckett, the first Chief Justice of Victoria.

In Europe he travelled widely and visited many medical centres. His first academic achievement was to obtain the doctorate in medicine of the University of Saint Andrews by special examination. The minutes of the University of Saint Andrews give the following details:

29th October 1853.

Dr. Day gave in an application from David John Thomas M.R.C.S. and John Mark Sutton M.R.C.S. for a special examination in Medicine on Monday first. The meeting agreed to the application, and the Examinations were fixed to commence on Monday evening at 7 o'clock.

The examiners were Dr. Day, Mr. Connell, and Dr. Pyper. The examination resumed the next day and lasted till late that evening. "Dr. Day then gave in the report of the examinations, recommending Mr. Sutton and Mr. Thomas for the degree of M.D. which was approved of; the Degree was accordingly conferred."

We can be sure that Thomas, while in Scotland, became acquainted with James Young Simpson. He had always maintained an interest in anæsthesia, and on his return he was, with Gillbee, one of the chief supporters of Simpson's methods, particularly of acupressure. Simpson was often quoted by Thomas, and one feels that he shows an enthusiasm for Simpson's work that was kindled by personal contact.

Thomas again visited Scotland in 1859, and later he reported on the follow-up of a patient upon whom he had operated in Melbourne in 1846 (Thomas, 1864*d*). On returning to London he obtained the Fellowship of the Royal College of Surgeons.

Thomas toured the Continent extensively in 1858. He studied anatomy and histology under Dr. Legendre in Paris, and performed "*avec une grande habilité toutes les opérations chirurgicales*". In the winter of 1858-1859 he did a course of four months at Heidelberg under Professor Nuhn. "He dissected with very great diligence, great perseverance and praiseworthy skill, all the different parts of the human body showing the highest proofs of his anatomical knowledge and much practical experience, which would highly fit him for the duties of a teacher in anatomy." (Thomas, 1860.) The course also included microscopic studies, in which he was always interested and about which he often spoke at medical meetings. His microscope is at present in the Museum of the Royal Australasian College of Surgeons. In his obituary notice in the *Australian Medical Journal* it is also stated that he studied in the principal cities of Holland, Switzerland and Italy (Neild, 1871).

Return to Victoria.

With his family he embarked from Liverpool on August 8, 1859, in the 1750-ton ship *Champion of the Seas*, which carried 259 migrants to Australia as well as a general cargo. She arrived in Melbourne on November 5, 1859, with a squally south-westerly wind blowing across the bay—a foreboding of the troubled times ahead for Thomas.

Things were different in the Colony of Victoria. Property values had depreciated, and Thomas's financial position was insecure. He had sold his property and furniture before leaving, and had lived expensively abroad. He was now forced to sell for £500 property for which he had previously refused £12,000. He had always been careless with money; his cash payments were deposited in convenient places about the house and promptly forgotten; he would accept and lose wagers on anything; and his generosity to the poor was renowned. It was left to Mrs. Thomas to collect the scattered money and bank it. She also infers in some of her letters that Barker had not managed the partnership to their mutual advantage while Thomas was away.

FIGURE II.

Photograph of the testimonial given to Thomas by his "brother practitioners" on his departure for England, February, 1853.

Practice itself had changed. There were now 600 doctors — a threefold increase since his departure — and many did not know his reputation. Competition was brisk and ethical standards were low. Thomas (1865*f*), in writing of the conditions of this time complained bitterly:

> There are an immense number of clubs, which are tendered for, and the lowest tender, of course, is taken . . . The standard of the profession is far below what it was when I formerly practised here . . . It is overcrowded; there is not a corner here where you will not find a medical man, and the means many adopt to gain patients is laughable. Actually, the wives of some men go about canvassing respectable pregnant women on behalf of their husbands . . . This is a capital country for quacks; the regular practitioner has no chance with them. I have a namesake here who advertised most unmercifully, which is many hundreds of pounds a year out of my pocket. Many patients are recommended to Dr. Thomas (from the country), and they invariably look for the address in the newspaper; they see his advertisement, and go to his rooms, where he pockets the fee that was intended for me.

In view of this, Thomas was forced to send the following disclaimer to *The Argus*:

> Notice
>
> A person in this city of the same name as my own has lately had his qualifications at the Colleges of Physicians and Surgeons of England, and the Medical Board of Victoria, erased from their registers.
>
> Finding that in this colony, where so many persons are strangers to each other, I have for years been, and am at present, in many instances confounded with this

person, much to my annoyance and detriment, I am, therefore, however objectionable it may appear, compelled, in order to correct this mistake, to resort to the measure I now adopt in publishing this notice. It has long been a painful affair to me that it should be supposed that I paraded my name in the newspaper and through handbills and placards; and it has lately become more so, that it should be falsely imagined that my name had been removed from the English and Victorian Medical Registers.

David John Thomas, M.D., Fellow of the Royal College of Surgeons, England, Member of the Medical Board of Victoria, Honorary Surgeon to the Melbourne Hospital.

129 Collins Street-East.

A combination of all these factors eventually led to his insolvency, which he declared in 1864. The declaration showed a deficiency of £7764 after stating his assets at £5831. The reasons given were the depreciation in value of real property and bad debts (*Australian Medical Journal*, 1866). Thomas was never to recover from this financial reverse.

Another tragedy occurred when, on September 6, 1862, Thomas's eldest daughter died, at the age of nineteen years, of prostration from ulceration of the small intestines, twenty-three days after the onset of typhoid fever. As a mark of respect to Thomas, the August meeting of the Medical Society of Victoria was cancelled because of a "severe domestic affliction in the family".

In spite of all these difficulties, Thomas reestablished his position by hard work. He topped the poll in the 1860 elections for the staff of the Melbourne Hospital and was soon taking an active part in hospital affairs. He held the position until his death, and in 1865 was chairman of the hospital staff. He became a member of the Medical Board of Victoria in 1865, and in 1868 was appointed official visitor to the Kew Asylum, and honorary physician to the Deaf and Dumb Institute and to the Saint James Training Institute. In that year he was appointed by the Crown Law Office to the roll of territorial magistrates. He was always a loyal and ardent Welshman, and in 1867 was the president of the annual Ballarat Eisteddfod (Thomas, 1867*f*).

In 1862 the medical school in the University of Melbourne was opened, and Thomas had the Melbourne doctorate of medicine conferred upon him *ad eundem gradum*. He became the first examiner in anatomy, and with Rudall set this university's first anatomy paper in 1862. This position was held by Thomas for three years.

His energy during these years was prodigious. The financial troubles did not seem to worry him, for their effect upon his work is only inferred. His name never appeared on the lists of donors to various charitable causes which occasionally appeared in the journal; nor was he prominent in social functions in this period.

In 1864 Thomas limited his practice to surgery because of the pressure of work. He therefore became the first specialist surgeon at the Melbourne Hospital.

The Medical Society of Victoria.

During his absence in Europe the Port Phillip Medical Association had died from natural causes, and in its place there grew a sickly infant, the Medical Society of Victoria. Thomas took a leading part in its activities, and in the early sixties it developed an appearance of permanency. He was elected vice-president in 1863 and president in 1864. At the monthly meetings he was a frequent contributor of papers on surgical topics, so practising what he had always maintained — that members should publish their work for the information and criticism of their fellows. Too often he was himself the blunt critic. In opening the discussion on a long paper in 1865, he "thought the Society much obliged to Dr. Mackenzie for the paper just read, although it was somewhat dry work listening to the details of cases". One wonders what the others thought of many of his papers, which were themselves very long and "somewhat dry work".

Nothing was more characteristic of the activities of the medical profession at this stage than its internal strife. The Medical Society of Victoria had its share, and the Society had many vehement critics outside its ranks, such as Thomson and Beaney, who contributed largely to the *Medical and Surgical Review* (*Australasian*). Thomas was often their target, and this was the case after the annual dinner of the Medical Society of Victoria in 1863. The *Australian Medical Journal* (1863) reported it thus:

> The utmost geniality and good feeling prevailed. The little professional differences which unfortunately insist upon intruding themselves into the ordinary experience of daily life, were by a kind of tacit consent forgotten for a time . . . The utmost point of merriment was reached when it was decided that the song must go round without exception.

The opposition, in their *Medical and Surgical Review* (*Australasian*), 1864-5, reported the occasion differently:

> The last bacchanalian revel of the Medical Society was held at Menzies Hotel last week. The gathering was not numerous. The proceedings were as usual. Appetites were solaced,—toasts drunk,—speeches made and songs sung. There was nothing worthy of notice, except an un-toe-ward movement on the part of the President of the Medical Society, who having ordered the waiters with coffee to leave the room, assisted the movements of one of them by an assault upon his tray. The cups and saucers flew in midair,—the sugar granules were made to frost surfaces not usually sweet,—the poor waiter "neat in vest and white cravat", lost for a moment the unpuckered cleanliness of his snowy linen. What next? Will anybody bring censure to bear upon this energetic dispenser of surgical amenities?

There were also differences of opinion within the Society, and no member was above severe criticism on occasions. Thomas's temperament was such that, although usually patient and full of bonhomie, he harboured several grudges. With Wilkie, once his great friend, relations were estranged. Perhaps Wilkie failed to enjoy the many jokes perpetrated at his expense. Halford was another for whom Thomas had little time. His persistent advertising of his availability for private consultation while holding a Chair at the University prompted Thomas's dislike. They lasted only two years together as coexaminers in anatomy.

Thomas, as president of the Medical Society of Victoria, did not always maintain the peace. At the September meeting in 1864 a motion which seemed to be directed against Dr. Wilson was put by Dr. Martin. This immediately caused uproar. The words "liar, scoundrel, vagabond were . . . flung about. But where was the President? He sat out the stupid episode with as much complacency as if it had been a pot-house brawl." (*Medical and Surgical Review* (*Australasian*), 1864-5.)

This rather violent meeting brought forth the article in the opposition's journal from which the foregoing is quoted. It was supposedly written by William Thomson, and it eventually led to Thomson's resignation from the Society under circumstances not to the credit of the president (Gandevia, 1953). During the debate on the authorship of the article Dr. Turnbull asked the president how he was sure that he (Turnbull) did not write it. Thomas replied: "I know you did not write it quite well. You have not the brains nor the ability to write it." Thomas's behaviour in like circumstances has been noted in a previous paper (Gandevia, B., 1954).

Apart from such lapses, Thomas worked untiringly for the Medical Society of Victoria. He was the most consistent contributor to the "Hospital Reports" in the journal, where his cases in the Melbourne Hospital were discussed. These cases showed how much he used his microscope in the study of his operation specimens. In one long and "somewhat dry" discourse he gave on the anatomical changes in the ovary associated with pregnancy it is evident that he kept pace with the latest overseas views (Thomas, 1866*d*). This paper was intended to clarify the conflicting ideas held by medical witnesses at the recent trial at which James George Beaney was successfully defended in the Supreme Court against a charge of having murdered one of his patients by performing an illegal

operation. Thomas was careful to draw no definite conclusions.

As retiring president of the Medical Society of Victoria he gave a long valedictory address in which he reviewed the changes in medical practice in Victoria as he had seen them. The settlement had grown from the "slab-huts" of the squatters to the durable mansions of mid-Victorian Melbourne. He strongly criticized the Melbourne Hospital's election system as one which "does not tend to raise the standards of the profession, either in a practical or scientific" manner. With this system "few men can even attain mediocrity". He pleaded for the development of specialist services "in order to keep pace with the profession", and concluded with another plea for members to "avoid all matters of a personal nature" (Thomas, 1865*b*). The latter was no doubt spoken with some feeling.

As a past president his interest in the Society did not flag, and in 1869 a unique tribute was paid to him. He was presented with a signed testimonial "expressive of the estimation in which he was held by the Society". This testimonial, beautifully illuminated on vellum by Messrs. Fergusson and Mitchell, read as follows:

> To DAVID JOHN THOMAS Esquire, M.D. St. And. et Melb., F.R.C.S.Eng., L.S.A.Lond, Surgeon to the Melbourne Hospital and formerly President of the Medical Society of Victoria, &c.
>
> Dear Sir,
>
> We the Members of the MEDICAL SOCIETY OF VICTORIA, have great pleasure, on the occasion of electing you an HONORARY MEMBER of the Society, in expressing the respect we entertain for you personally and the high opinion we hold of your great skill as an accomplished surgeon. Your long and honorable career in the Colony and your close identification with every movement relating to the interests of the profession are part of the history of this rapidly advancing community; and your many valuable contributions to the literature of medicine will always be remembered with gratitude by those who regard such records as the materials out of which the science of medicine is constructed.
>
> Permit us to assure of our warm esteem and sincere admiration and to remain,
>
> With the most cordial feelings of professional brotherhood,
>
> Faithfully yours,
>
> (Signatures.)

The report of the meeting (*Australian Medical Journal*, 1870) continued as follows:

> Dr. Thomas, in replying said that . . . he was deeply conscious of the high compliment the Society had paid him. He had always loved the profession, and therefore such services as he had rendered the Society were but the expression of his love for the art he practised.

At this time Thomas, Wilkie, Black, and Campbell were the only survivors of the pioneering practitioners of the early forties; and Thomas was the established leader of the profession in Melbourne and the senior surgeon to the Melbourne Hospital.

Surgery.

During the sixties his surgical work continued to occupy most of his time. His frequent operation reports in the journal show the breadth of his practice. Orthopædic operations were the commonest "capital" procedures, and the excision of joints for ankylosis was in vogue. Amputations were still a part of everyday surgery, as were lithotomy and herniotomy. Thomas was by this time one of the older group of surgeons who were slow to realize the full impact of Lister's work on surgery. He had accepted it in part, using carbolic in only two reported cases, and in these he used it inadequately, as though paying lip service to the new regime. Revolutionaries are usually younger men than Thomas was in 1867. His surgery had already brought him the respect of the community.

Death.

With this place of eminence in the profession established after long years of hard work there is little wonder that Thomas's health began to fail in his late fifties. By 1871 it was obvious to his friends that his physical energy was not as great as usual. He had suffered "occasional impairment of motor power, indicating impending paralysis", but his intellectual faculties remained unimpaired. On June 1, 1871, while preparing to go to the hospital to operate, he suffered a major stroke and soon became comatose. Six hours after his right arm had dropped helpless to his side he was dead. He left only £500 for his wife and four surviving daughters; and with characteristic casualness toward money matters he died intestate. A large body of the medical profession and other distinguished citizens attended his funeral at the General Cemetery on June 3.

So died David John Thomas, a loyal Welshman, "a cheerful, impulsive, warm hearted man, with a vivid sense of humour", a surgeon of note whose diagnoses were "singularly accurate", and whose "system of treatment was distinguished by its simplicity". He was the first in our profession who stood out above his fellows—surely "one of the founders of Victorian medicine" (Neild, 1871).

Acknowledgements.

In preparing a paper such as this one inevitably needs help. I would like to thank all those who have made this work possible and, in particular, Dr. H. Boyd Graham, Dr. Bryan Gandevia, Mr. R. M. Jukes, Miss Booth, Librarian of the Medical Society of Victoria Library, and Mr. Cottier, of the Victorian Eye and Ear Hospital.

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(1864), *M. & Surg. Rev.* (*Australasian*), 2: 108, 210, 226 (concerning his chairmanship of the Medical Society of Victoria meeting and the *Melbourne Hospital Incorporation Act*).
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(1867), *Australian M. J.*, 12: 96 (on colonial fever) and 219 (on Halford's treatment of snake-bite).
(1868), *Australian M. J.*, 13: 333 and 368 (on the Melbourne Hospital Committee interfering with the management of patients).
(1869), *Australian M. J.*, 14: 159 (on Halford's treatment of snake-bite).

4. *Contributions to Discussion.*

This list is compiled from the reports of the meetings of the Medical Society of Victoria, and mentions only his more important contributions

1864, Ovariotomy, Fractures, Gangrene.
1865, Typhus and Typhoid, Intussusception, *Morbus Addisonii.*
1866, Lithotomy, Sanitation.
1867, Chloroform in Convulsions, Erysipelas.
1868, Scurvy, Listerism, Spinal Deformities, Diphtheria.
1869, Colonial Fever.
1870, Consumption, Snake-Bite, Laudanum Poisoning, Erysipelas, Varicocele.

THE ROLE OF SULPHONYLUREA DERIVATIVES IN THE MANAGEMENT OF DIABETES MELLITUS: A PRELIMINARY REPORT.

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From the Diabetic and Metabolic Unit, Alfred Hospital, Melbourne.

IN 1942, Janbon and his associates reported that p-amino-benzene-sulphonamido-isopropyl-thiadiazole reduced the blood sugar content of animals to hypoglycæmic levels. A similar activity was shown by many of the p-amino-sulphonamido-alkyl-thiadiazoles in the experiments of Loubatières (1944*a* and *b*, 1946) and Bovet (1944). However, the non-sulphonamido-thiadiazoles proved to have no such hypoglycæmic action. Recently, Achelis and Hardebeck (1955) have shown that another sulphonamide derivative, 1-butyl-3-p-amino-benzene-sulphonylurea, produces hypoglycæmia in animals and in healthy human beings. Franke and Fuchs (1955) have studied the action of this compound in diabetic patients, and state that it lowers the level of blood sugar, reduces glycosuria and in some instances can replace insulin therapy. Bertram, Bendfeldt and Otto (1955) have reported significant success in clinical trials of this drug which they have administered to a large group of patients for many months. It is apparent from their reports that the middle-aged obese patient responds satisfactorily, but the young patient and the "brittle" patient are uninfluenced, even by large doses.

In recent months 1-butyl-3-p-amino-benzene-sulphonylurea, BZ-55 or "Carbutamide" (Lilly) has been subjected to intensive investigation in the United States of America (Ridolfo and Kirtley, 1956), Canada and Great Britain. Another compound, 1-butyl-3-p-toluene-sulphonylurea, "Orinase" (Upjohn), has also been shown to possess hypoglycæmic activity (Miller and Craig, 1956). Reports of clinical trials with both these sulphonylureas have provided results which are sufficiently encouraging to warrant further investigation.

Mode of Action.

Loubatières (1944*a*) noticed that p-amino-sulphonamido-isopropyl-thiadiazole produced hypoglycæmia in normal and

in partially depancreatized dogs, but that it had no effect in totally depancreatized dogs. This led to the suggestion that it might act by stimulating insulin secretion. Chen, Anderson and Maze (1954) reported that it had no hypoglycæmic action in alloxan diabetic rabbits, a finding which has been confirmed with the more recently developed compounds. Holt, Holt, Kröner and Kühnau (1954*a* and *b*) reported that p-amino-sulphonamido-isopropyl-thiadiazole produced severe degenerative changes in the *a* cells of the islets of Langerhans in rabbits. From this they concluded that the action of the sulphonylurea compounds was concerned with an inhibition of glucagon secretion. This has not been confirmed by American workers. Mirsky, Perisutti and Diengott (1956*a* and *b*) have suggested that the hypoglycæmic action of these sulphonamides is due to a non-competitive inhibition of insulinase with a consequent decrease in the destruction of endogenous insulin. Miller and Dulin (1956), comparing the action of "Orinase" and insulin in intact fasting Sprague-Dawley rats, have shown that liver glycogen is increased while muscle glycogen is unchanged in "Orinase"-treated animals. By contrast, muscle glycogen is increased with no significant increase in liver glycogen in animals treated with insulin. Experiments on glucose utilization by isolated muscle and on lipogenesis by liver slices indicate that these compounds possess no insulin-like activity (Krahl, personal communication). Krahl (personal communication) has shown that glucose utilization by brown fat is substantially accelerated in the presence of BZ-55, which is more effective in this regard than insulin. Another interesting finding is the absence of any hypoglycæmic effect in hepatectomized animals (Stadie, personal communication).

At the present time there is insufficient evidence on which to base any conclusions on the pharmacological action of these compounds. It seems unlikely that they can be considered as "insulin substitutes", and their exact mode of action and the manner in which they affect the disturbed metabolic processes of *diabetes mellitus* will be determined only by further study.

Empirical Considerations.

Screening experiments in animals have failed to show any serious side effects from the continuous administration of these sulphonylureas in high doses over long periods of time. There is no demonstrable effect upon the liver or kidneys, and little effect upon the activity of bone marrow. In rare instances human patients have developed leucopenia which disappeared with reduction in dosage of the drug (Franke and Fuchs, 1955). A few skin rashes of the typical sulphonamide type have been reported.

Bertram, Bendfeldt and Otto (1955, 1956) suggest, as a result of their clinical trials with human patients, that a considerable variation in response can be expected. The dosage which they recommend is 2·0 to 4·0 grammes on the first day of treatment followed by a daily maintenance dose of 1·0 to 2·0 grammes. Middle-aged obese patients show the best response, particularly if the diabetes is of short duration. Some of these patients have been able to discontinue insulin without any return of glycosuria or hypoglycæmia. Some patients on ceasing treatment with sulphonylurea have remained in satisfactory diabetic control with diet alone for many weeks, whereas prior to treatment dietary measures had failed to control the disease. With younger patients the response has been less satisfactory, many showing no reaction even to large doses. These drugs have no demonstrable effect in the presence of ketosis and are quite unsuitable for the treatment of any diabetic emergency. The suggestion has been made that, because of the inability of these drugs to influence diabetes in alloxanized or pancreatectomized animals, they are likely to be effective in obese insulin-resistant patients, but not in thin insulin-deficient patients.

With the dosage recommended an adequate plasma sulphonamide level of eight to ten milligrammes per 100 millilitres is reached within twelve to twenty-four hours, and this can be maintained in most patients with a daily dose of 1·0 to 2·0 grammes. The drug is excreted slowly and disappears completely from the circulation about ten

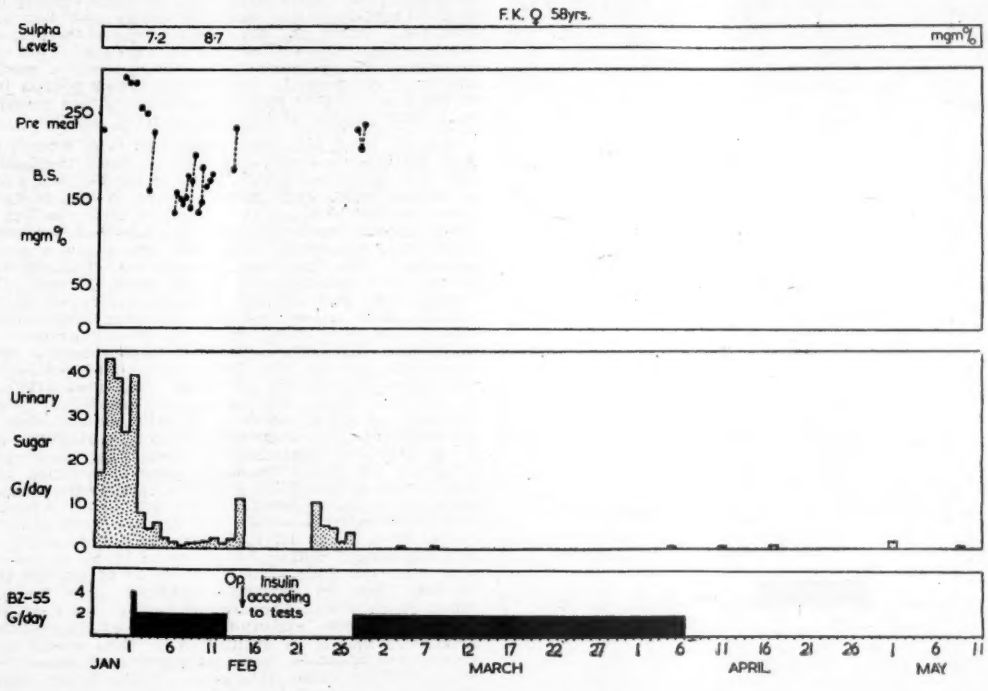

FIGURE I.

days after oral administration is stopped. There is apparently little danger of crystalluria even after prolonged administration. With the doses recommended patients experience very few untoward symptoms, although with higher doses nausea, headache, tremor and sweating have been noticed on occasions.

Case Records.

During the past three months 14 patients attending the Diabetic and Metabolic Clinic of the Alfred Hospital have been treated with 1-butyl-3-p-amino-benzene-sulphonylurea

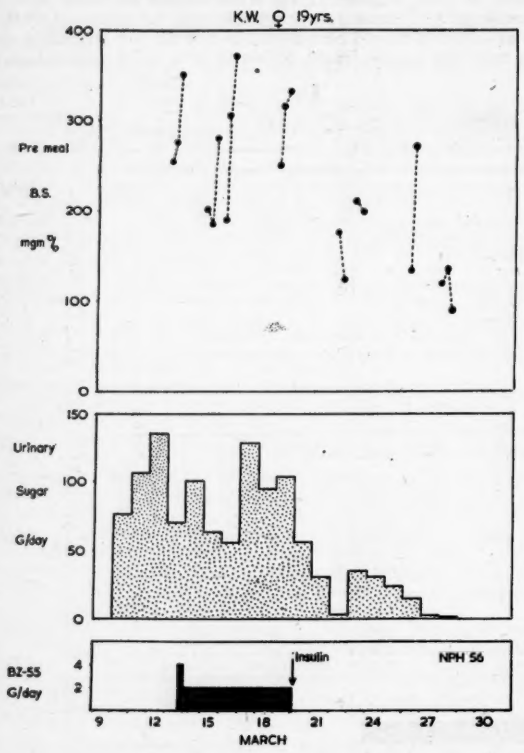

FIGURE II.

("Carbutamide"). These patients have been selected for trial in the light of German experience and have been studied with particular reference to the presence or absence of insulin in the blood-stream. An outline of the results obtained in this series is given in Table I. Details of the response of six of these patients are given in the following clinical notes.

Mrs. A., aged fifty-eight years, developed symptoms of diabetes three months before the period of clinical trial. Her mother and two sisters were known to suffer from diabetes. Physical examination revealed no obvious abnormality apart from genital prolapse. Her weight was 137 pounds. Insulin was demonstrated in her blood plasma. She was admitted to hospital, and while on a 1500 Calorie diet her daily excretion of glucose varied between 30 and 37 grammes. Blood sugar estimations during this period were in the vicinity of 280 milligrammes per 100 millilitres. Six days after admission to hospital she was given an initial dose of 4·0 grammes of BZ-55 followed by a daily maintenance dose of 2·0 grammes. The daily urinary excretion of glucose promptly fell to 8·0 grammes and later to 1·0 gramme. Thirteen days after commencement of BZ therapy she underwent an operation for genital prolapse. At this juncture the administration of BZ-55 was discontinued and her diabetes was controlled with appropriate doses of regular insulin. For two days after the operation her urine contained appreciable amounts of acetone. Fourteen days after the operation BZ-55 therapy was recommenced and her twenty-four hour excretion of glucose in the urine soon fell to less than 1·0 gramme. After thirty-eight days BZ-55 was again discontinued, and for the next six weeks the patient was treated with a 1500 Calorie diet alone. She remained well, and the output of glucose in her urine was consistently less than 1·5 grammes per day.

Miss B., aged nineteen years, developed thirst, polyuria and recurrent boils twelve months before the period of clinical trial. During this time she received no treatment and lost 30 pounds in weight. Tiredness, anorexia, nausea and *pruritus vulvæ* were prominent symptoms prior to her admission to hospital. Examination showed her to be a thin apathetic girl whose urine contained large amounts of sugar and acetone. Her weight was 115 pounds. Insulin was present in her blood plasma. During the preliminary period of observation her daily average urinary excretion of glucose was 87 grammes. Eight days after her admission to hospital BZ-55 therapy was commenced with an initial dose of 4·0 grammes followed by daily maintenance doses of 2·0 grammes. During the next week the daily urinary output of glucose remained the same as before and her symptoms persisted. After ten days sulphonamide therapy was discontinued and she was treated with insulin. This caused an immediate disappearance of acetonuria and a rapid fall in the blood sugar level. She gained seven pounds in weight in the first week of insulin therapy and has remained well on a daily dosage of 56 units of NPH insulin.

Mrs. C., aged fifty-nine years, had been known to suffer from diabetes for four years. Her condition had been reasonably well controlled with a 1900 Calorie diet and a daily dose of insulin which had varied between 28 and 40 units. For three months prior to the period of trial she had suffered from mental depression and was admitted to hospital for psychiatric treatment. To this she made a satisfactory response. She was then studied for response to BZ-55. Insulin was demonstrated in her blood plasma. Her daily insulin dose was stopped and she continued to take her original diet. After some days her preprandial blood sugar estimations gave values of 385 to 540 milligrammes per 100 millilitres. Her urine contained a considerable amount of sugar and acetone, the daily excretion of glucose being in the region of 80 to 100 grammes. One week after cessation of insulin therapy she was given an initial dose of 4·0 grammes of BZ-55 followed by daily maintenance doses of 2·0 grammes. Her response was not satisfactory, and eight days later the maintenance dose was increased to 4·0 grammes per day. The daily urinary excretion of glucose fell to the range of 10 grammes, and there was a simultaneous fall in the level of the blood sugar. At the time of her discharge from hospital the diurnal range of blood sugar varied from 130 to 225 milligrammes per 100 millilitres. She was discharged taking 3·0 grammes of BZ-55 per day. At this stage the daily urinary excretion of glucose had fallen to less than 1·0 gramme. Shortly after her discharge BZ-55 therapy was discontinued and for the next five weeks the daily glucose excretion remained at approximately one gramme. She is in good health. Two weeks after commencement of BZ-55 therapy the white cell count fell to less than 2000 per cubic millimetre. Without any alteration in BZ-55 dosage or any specific therapy, this returned to normal limits and has remained so ever since.

Mr. D., aged sixty-five years, developed symptoms of diabetes two years before the period of clinical trial. His condition had remained under satisfactory control with an appropriate diet until one month before his admission to hospital. For no obvious reason he then felt tired, became thirsty and lost 14 pounds in weight. At the time of his admission to hospital physical examination revealed no significant abnormality other than obesity (his weight was 159 pounds). After seven days of strict diet his blood sugar values ranged between 195 and 295 milligrammes per 100 millilitres. His daily urinary excretion of glucose was 17 grammes per day. He was then given an initial dose of 4·0 grammes of BZ-55 followed by a daily maintenance dose of 2·0 grammes. There was an immediate improvement in his subjective condition, and his daily excretion of glucose dropped to 1·5 grammes. Shortly after commencing BZ-55 therapy, he developed a papular rash on the face which disappeared spontaneously. He has been maintained on 2·0 grammes of BZ-55 daily and has remained well, his urinary excretion of glucose each day being less than 2·0 grammes. No estimation of plasma insulin was made in this patient.

Mrs. E., aged sixty-seven years, complained of tiredness, loss of weight and thirst for six months prior to her admission to hospital. For six weeks prior to the period of trial she took a 1900 Calorie diet which failed to control her glycosuria. Examination revealed no significant abnormality. Her weight was 137 pounds. Her daily excretion of glucose

TABLE I.

Patient.	Age. (Yrs.)	Sex.	Weight. (Pounds.)	Duration of Diabetes.	Previous Treatment.	Mean Urine Glucose Excretion. (Grammes per Day.)			Blood Sugar Content. (Milligrammes per 100 Millilitres.)		Other Features.	Insulin in Plasma.	Success or Failure.
						Before BZ Therapy.	During BZ Therapy.	After BZ Therapy.	Before Therapy.	After Therapy.			
C.	59	F.	147	4 years; recent ketosis.	Insulin, 28–40 units daily.	95·0	50·0 (2·0 grammes per day) 10·0 (4·0 grammes per day).	0	385–540	130–215	Three months' depressive state. Leucopenia (2000 per cubic millimetre) but returned to normal without alteration in dose.	Present.	Success.
E.	67	F.	143	6 weeks.	1900 Cal. diet.	13·0	7·0 (2·0 grammes per day). 2·0 (4·0 grammes per day).	13·0	200–240	120–160	——	Present.	Success.
F.	69	F.	153	18 months.	1500 Cal. diet.	38·0	9·0 (2·0 grammes per day). 15·0 (4·0 grammes per day).	—	250–325	140–250	Retinitis. Photosensitive rash 16 days after treatment commenced; responded to antihistaminics. No porphyrinuria.	Not estimated.	Failure.
G.	40	M.	166	6 weeks.	Ketosis; given insulin.	—	1·0	1·0	265	90–110	——	Present.	?
H.	51	F.	144	6 years; 2 months unstable.	1500 Cal. diet.	68·0	18·0 (2·0 grammes per day). 5·5 (4·0 grammes per day).	—	280–350	155–210	Rash on face and *otitis externa* 27 days after therapy commenced. Rash faded with local applications.	Not estimated.	Success.
B.	19	F.	115	1 year.	None.	87·0	91·0	—	255–380	250–330	Asthma. Dysmenorrhœa. Recurrent chest infections.	Present.	Failure.
D.	65	M.	159	2 years; 6 months unstable.	1500 Cal. diet.	17·0	1·5	—	195–295	125–190	Rash on face, neck and legs four days after therapy commenced; cleared in 24 hours.	Not estimated.	Success.
I.	59	F.	167	8 years; 10 months unstable.	1500 Cal. diet.	45·0	26·0 (2·0 grammes per day), 7·0 (4·0 grammes per day).	—	270–300	135–180	Previous sensitivity to sulpha drugs. Hypertensive and mild congestive cardiac failure. Rash 10 days after therapy commenced. Dose reduced.	Not estimated.	Success.
A.	58	F.	137	3 months.	1100 Cal. diet.	37·0	3·0	1·0	285–290	135–180	Family history of diabetes—mother and two sisters. Operation performed during stay in hospital; required small amounts of insulin.	Present.	Success.
J.	52	F.	154	2 years.	20 units of insulin.	—	—	—	295–320	125–190	Insulin allergy. Treated with E.C.T. for depressive state, with improvement.	Not estimated.	Success.
K.	59	M.	190	16 years.	160 units of insulin.	106·0	76·0	—	270–355	265–320	Acromegaly. Taken off insulin.	Present.	Failure.
L.	64	F.	—	20 years; 1 year unstable.	1500 Cal. diet.	31·0	16·0 (2·0 grammes per day). 15·0 (4·0 grammes per day).	—	255–325	165–270	Patient blind.	Not estimated.	Failure.
M.	64	M.	242	7 years; 3 months unstable.	1500 Cal. diet.	—	—	—	280–330	170–210	Peripheral neuritis.	Not estimated.	Success.
N.	63	F.	147	3 months.	1500 Cal. diet.	—	—	—	230–290	—	Eczema of legs.	Not estimated.	Success.

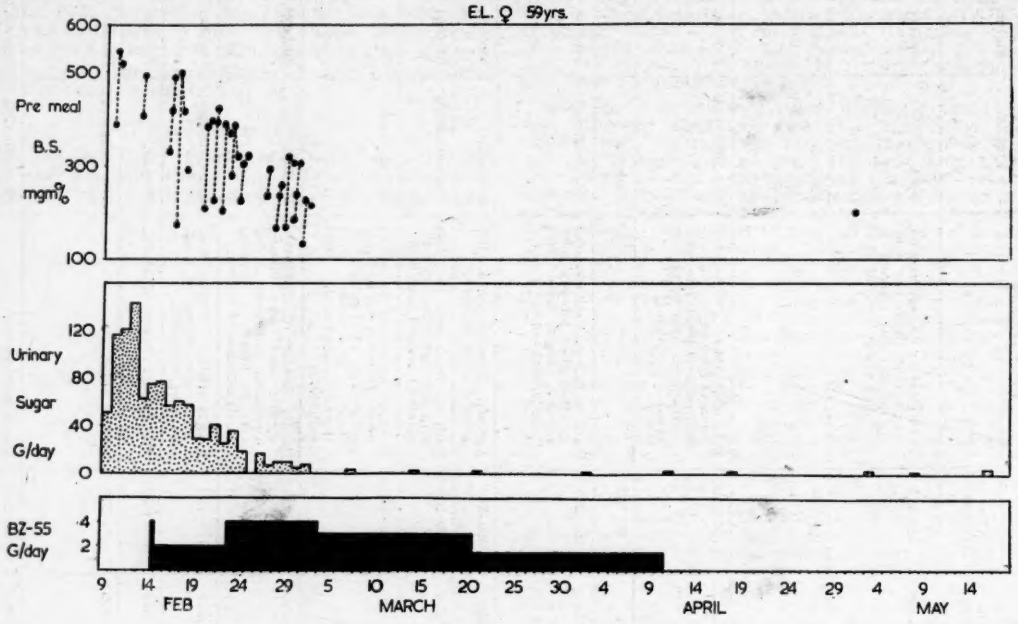

FIGURE III.

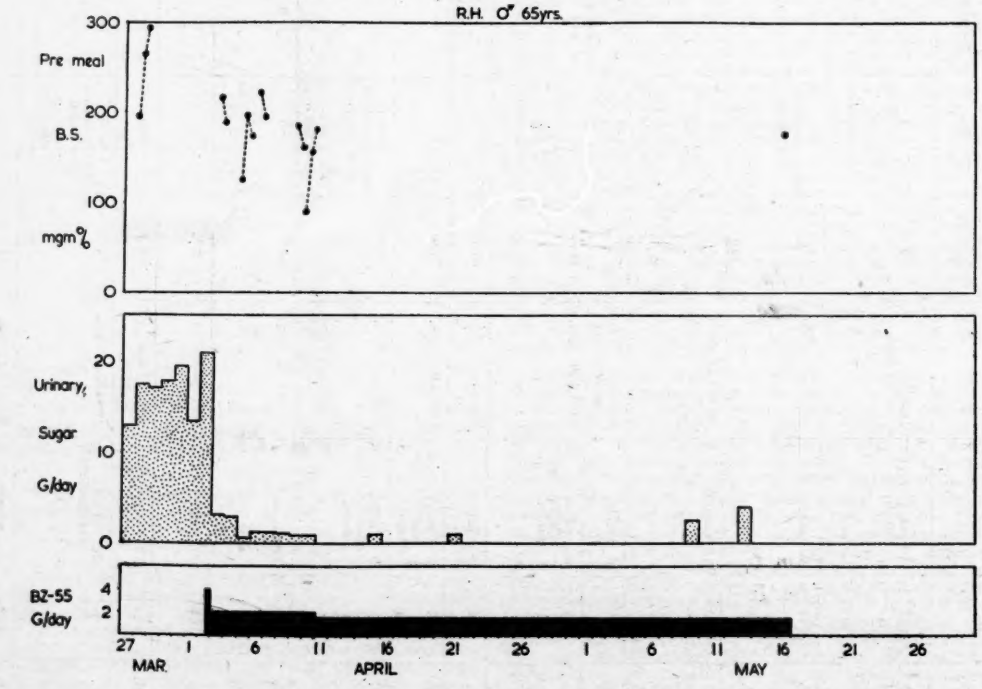

FIGURE IV.

in the urine was 13 grammes and her blood sugar estimations ranged between 200 and 240 milligrammes per 100 millilitres. Insulin was demonstrated in her plasma. Eight days after her admission to hospital BZ-55 therapy was commenced with an initial dose of 4·0 grammes and maintenance doses of 2·0 grammes. Seven days later, because of an inadequate response, the daily maintenance dose was raised to 4·0 grammes. Her daily urinary excretion of glucose promptly fell from 7·0 grammes to an average of 2·0 grammes. Three weeks after admission she was discharged from hospital on a dose of 3·0 grammes BZ-55 each day. At the time of discharge she felt well, she was less tired and her appetite

had increased. Two days after the initiation of BZ-55 therapy her blood sulphonamide concentration was 7·6 milligrammes per 100 millilitres, and on the tenth day it was 9·2 milligrammes per 100 millilitres. After her discharge from hospital the daily urinary excretion of glucose varied between 0·5 and 1·0 gramme. Six weeks later BZ-55 therapy was discontinued and within the next ten days the daily urinary excretion of glucose rose to 18 grammes. BZ-55 therapy was then resumed and she again responded satisfactorily.

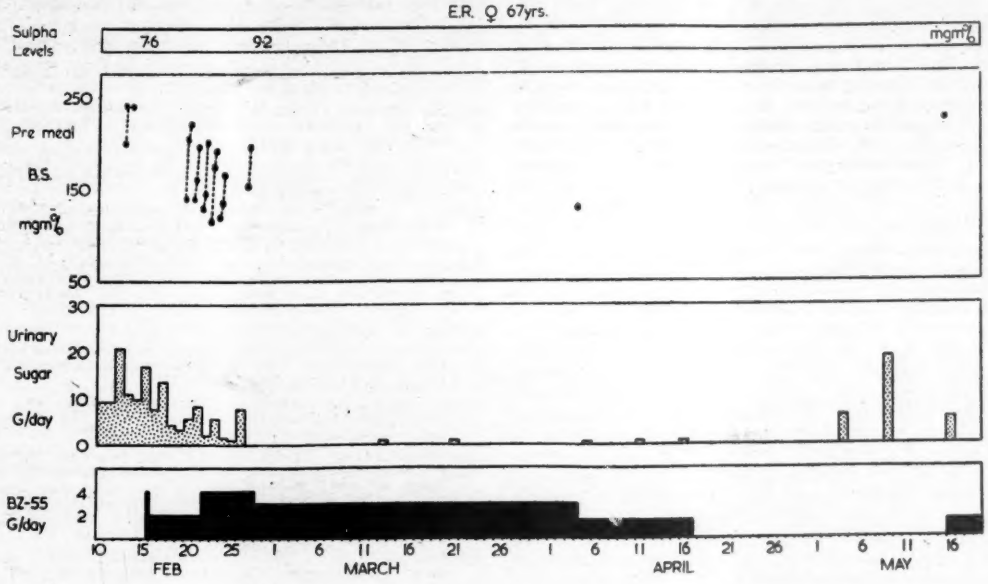

FIGURE V.

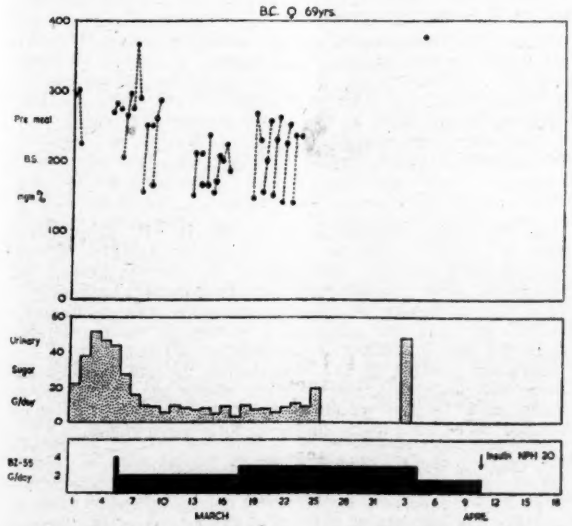

FIGURE VI.

Mrs. F., aged sixty-nine years, was known to have suffered with diabetes for two years prior to the period of observation. For nine months before her admission to hospital she had been taking a 1500 Calorie diet which abolished her symptoms of thirst and tiredness, but she had continuous glycosuria and her blood sugar values ranged between 250 and 325 milligrammes per 100 millilitres. Examination revealed no significant abnormality, but typical diabetic retinopathy was present. Her weight was 153 pounds. The total daily urinary excretion of glucose was 40 grammes. Ten days after her admission to hospital BZ-55 therapy was commenced with an initial dose of 4·0 grammes and a daily maintenance dose of 2·0 grammes. Eleven days later the urinary excretion of glucose was 7·0 grammes and the dose of BZ-55 was then increased to 3·0 grammes per day. Her blood sugar values fell to a diurnal range of 140 to 250 milligrammes per 100 millilitres, but there was little significant change in the daily excretion of glucose. BZ-55 therapy was discontinued, and after her discharge from hospital the urinary excretion of glucose rose to approximately the same figure as before her admission. Subsequently her condition was brought under satisfactory control with a daily dose of 24 units of isophane insulin. It is interesting to record that eight days after commencing treatment with BZ-55 she developed a follicular rash on exposed parts of her body—face, hands, forearms, legs and the dorsal aspects of the feet. It appeared to have a photosensitive distribution and disappeared after the application of antihistamine ointment. No estimation of plasma insulin content was made.

Discussion.

The mode of action of the sulphonylurea compounds upon the disturbed metabolic processes of *diabetes mellitus* is as yet unknown (Editorials, 1955, 1956*a*, *b*, *c*, *d*). Although they apparently have the effect of lowering the level of blood sugar and of reducing the excretion of glucose by the kidney in some patients, it cannot be assumed that these results are achieved by an action similar to that of insulin. The complete lack of response of the alloxanized or pancreatectomized animal suggests that these compounds can in no way be regarded as insulin substitutes. The failure of some human patients, whose plasma contains appreciable amounts of insulin, to show a satisfactory response to treatment with sulphonylurea compounds suggests that they do not act by facilitating insulin action. Further studies which are now proceeding on certain types of insulin-resistant patients may clarify this view, but at the present time it seems unlikely that they have any influence upon insulin-resistant patients who have demonstrable insulin in their plasma.

It seems obvious that further knowledge of the mode of action and some simple means of determining the response of patients are neecssary before these compounds can be

recommended for general use in the treatment of *diabetes mellitus*. While it seems that there is little danger from the recognized risks of prolonged sulphonamide therapy such as agranulocytosis, other side effects await explanation. Some patients who have shown response to BZ-55 therapy become hyperglycæmic and have glycosuria ten days after cessation of treatment. This corresponds to the time required for the excretion of the drug from the blood-stream. Others respond differently, and no glycosuria or hyperglycæmia is found for weeks after cessation of treatment. Far from being considered a satisfactory result of therapy, this finding is sufficiently disquieting to raise the suspicion of some sinister interference with metabolic processes and to pose the question of possible hepatic damage in a form as yet unrecognized. Experience with "Synthalin" some years ago lends support to the contention that premature acceptance of chemotherapy in the control of *diabetes mellitus* is apt to be followed by unsuspected and unfortunate consequences.

At the present time there is potential danger in the indiscriminate use of these compounds except under strict observation and biochemical control. The sudden cessation of insulin therapy and its replacement by any form of oral therapy particularly in any young or thin insulin-sensitive patient is likely to be followed by severe ketosis and critical consequences. Further experience is necessary before the place of these compounds in the treatment of *diabetes mellitus* can be determined.

Summary and Conclusions.

From a brief and limited experience of the use of a sulphonylurea compound, BZ-55 ("Carbutamide"—Lilly), the following observations have been made.

There appears to be an appreciable variation in the response of patients to the exhibition of this drug when given in the recommended dosage.

This variation in response does not seem to be related to the presence of insulin in the blood plasma.

The observation of Benfield *et alii* that an appropriate level of sulphonamide in the blood is necessary for a proper therapeutic response is supported.

Some patients, after cessation of BZ-55 treatment, have remained in proper control (as judged by blood sugar estimations and estimation of the daily excretion of glucose) for periods of many weeks, whilst others have shown a return of glycosuria and hyperglycæmia within ten to fourteen days.

There appears to be no simple or satisfactory test at present which would enable one to predict which patients are likely to respond to BZ-55 therapy.

Acknowledgement.

It is desired to acknowledge our appreciation for the invitation of the Research Division of Eli Lilly Company Proprietary, Limited, to participate in clinical trials of BZ-55 and for the provision of supplies of this substance and financial assistance. We are especially grateful to Dr. Franklin B. Peck, senior, and to Dr. W. Kirtley for their encouragement and criticism and for the information they have supplied on current research in the United States of America on this subject.

The technical assistance of Miss Diane van Assche is gratefully acknowledged.

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ANTICOAGULANTS.[1]

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Sydney.

IN the short time available to me it will be possible only to cover certain aspects of anticoagulants. These aspects will be the following: (i) the pathology of atheroma, with special reference to coronary atheroma; (ii) the pathology of phlebothrombosis and pulmonary embolism; (iii) the mechanism of normal blood coagulation, the site of action of therapeutic anticoagulants, the laboratory control of the coagulation defects induced by these anticoagulants, the rationale of the use of anticoagulants, and finally certain laboratory tests which were alleged to be diagnostic of thrombotic phenomena.

Pathological Background.

Atheroma.

Atheroma consists of patches of thickening of the intima of arteries, in which the deeper layers of the intima show deposits of lipoid material, which contains mainly cholesterol and cholesterol esters, but also phospholipids, fatty acids and lipo-proteins. Overlying these lipide accumulations there is a layer of hyalinized collagenous connective tissue covered by vascular endothelium.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on November 24, 1955.

Only atheroma of coronary arteries will be considered because of the widespread use of anticoagulants in this disease.

The study of autopsy material from patients dead primarily of diseases other than coronary atheroma reveals an extremely high incidence of extensive coronary atheroma. The lesions found in most of these patients represent early coronary atheroma, which is hard and sclerotic without necrotic softening. Thrombosis and intimal hæmorrhage are rare, and in only a small proportion of cases is the size of the lumen greatly reduced. This foregoing state may be referred to as stable atheroma, and it is immediately important only because of the great narrowing of the lumen in some of the cases. The important lesions of atheroma—that is, important in regard to the integrity of the myocardium—may be considered as complications of the foregoing stable state. The important change from this stable state is the occurrence of necrotic softening of the atheromatous plaque. This process of softening spreads to the endothelial surface causing destruction of the endothelium with one or more of the following results: (i) thrombosis occurring on the damaged endothelial surface; (ii) the discharge of atheromatous debris into the lumen, which debris may occlude the distal branches of the artery, (iii) intimal rupture causing the formation of an intimal flap which may partly or completely occlude the lumen; (iv) intimal hæmorrhage. Various combinations of the above-mentioned four phenomena may occur.

There has been much discussion of the part that intimal hæmorrhage plays in occlusive coronary artery disease. Three different modes of pathogenesis have been described. The first is that the hæmorrhage seen in the intima is the result of entry of blood from the lumen through the damaged endothelium into the softened atheromatous plaque. In other words, the atheromatous contents of the plaque are replaced by blood from the lumen. The second is that hæmorrhage occurs into the atheromatous plaque from capillaries of the *vasa vasorum*, which in atheroma penetrate to the deeper layers of the intima. The capillaries are involved by the necrotic softening process, and thus hæmorrhage occurs from them. The third is that in atheroma capillaries may pass from the endothelium of the intima down through the superficial layers of the intima to the atheromatous plaque, and that from these capillaries, which become involved in the necrotic softening process, hæmorrhage occurs. From the recent studies of Drury it seems likely that the last two sources of intimal hæmorrhage do not commonly occur, and that when hæmorrhage occurs from either of these two groups of capillaries it is insufficient in amount to cause any real diminution in the lumen of the vessel. This may be anticipated when one considers the low pressure present in these capillaries. The formation of an expanding intimal hæmatoma against the relatively high coronary artery pressure would seem unlikely. Hæmorrhage from these capillaries does definitely occur, but it seems unlikely that such hæmorrhage contributes to occlusion of the vessel in the great majority of cases. Thus it would appear that hæmorrhage into an atheromatous plaque through a damaged superficial intima is the usual cause of intimal hæmorrhage, and it has also been shown that this process of intimal hæmorrhage, which is secondary to necrotic softening of the intimal atheromatous plaque with destruction of the endothelium, is not in itself a factor of importance in producing either coronary thrombosis or diminution of the coronary lumen. From the foregoing it can be seen that intimal hæmorrhage is not a valid contraindication to the use of anticoagulant therapy.

In summary, it may be said that necrotic softening of an atheromatous plaque involving the endothelium initiates a variety of processes which all result in considerable diminution of coronary lumen, this in turn often resulting in myocardial infarction. These processes are (i) thrombosis, (ii) the discharge of atheromatous debris into the lumen which may occlude distal branches, and (iii) the formation of an intimal flap.

In patients with coronary atheroma and myocardial infarction, thromboembolic phenomena occur and may be divided into intracardiac and extracardiac groups. In the intracardiac group we have the following: (*a*) extension of the original coronary thrombus; (*b*) formation of new coronary thrombi in the same branch of the coronary artery or in another branch of the coronary arteries; (*c*) mural thrombi (17% to 18% of autopsies in such cases) forming in ventricles, giving rise to emboli which may be systemic or pulmonary.

In the extracardiac group we have phlebothrombosis of the deep veins of the pelvis and lower extremities (occur in 25% to 70% of autopsies in such cases) and pulmonary emboli arising from these areas of phlebothrombosis. Pulmonary embolism has been reported in 3% to 42% of subjects dead of myocardial infarction.

It will thus be seen that thromboembolic phenomena contribute greatly to the morbidity and mortality of coronary atheroma complicated by myocardial infarction. It would seem reasonable, therefore, that any attempt to prevent the occurrence or the spread of thrombosis by safe therapeusis is justifiable.

Phlebothrombosis.

Quick in 1951 suggested the use of the term "phlebothrombosis" to indicate thrombosis occurring in deep veins where the thrombosis was not secondary to acute inflammation of the wall of the vein. The latter condition we all know as thrombophlebitis, and it will not be discussed here.

Phlebothrombosis usually occurs in patients over the age of thirty years, and these patients may be divided into the following groups: (i) post-operative patients (those recovering from major operation, usually abdominal or pelvic operation); (ii) post-partum patients; (iii) patients with congestive cardiac failure or other diseases giving rise to chronic venous congestion; (iv) patients with carcinomatosis or other disseminated malignant disease; (v) any patient confined to bed for more than a short period. Many factors contribute to the occurrence of phlebothrombosis, and it is probably an accumulation of adverse circumstances rather than one particular change in the composition of the blood or structure of the vein wall which results in phlebothrombosis. In the post-operative and post-partum patient the following changes have been found (Wright, 1954): (*a*) The platelet count rises from an average of 300,000 to a peak of 700,000 per cubic millimetre on the tenth post-operative day and returns to normal on the twentieth day. (*b*) The stickiness of platelets—that is, their tendency to adhere to a water-wettable surface—increases to a maximum at the tenth day and decreases to normal on the twentieth day. (*c*) The foot-groin venous flow time actually decreases during the first two post-operative days, but then increases to a maximum of approximately twice the normal time at the eleventh post-operative day, returning to normal on the twenty-first post-operative day. The incidence of phlebothrombosis is maximal at the time when the levels of the above-mentioned factors are also at their peak. Thus from the foregoing it has been assumed that the following are factors of importance in post-operative and post-partum phlebothrombosis (groups (i) and (ii) above): (*a*) diminished rate of venous blood flow; (*b*) increased concentration of platelets in the blood; (*c*) increased "stickiness" of the platelets.

With regard to groups (iii), (iv) and (v) above—patients with chronic venous congestion or disseminated malignant disease or patients merely confined to bed—it is likely that the three factors mentioned above, (*a*), (*b*) and (*c*), also occur, especially (*a*)—that is, diminished rate of venous blood flow.

In any discussion of phlebothrombosis it has been assumed that there is an endothelial defect which presents a water-wettable surface on which thrombosis can occur. Very little is known of the nature of the endothelial lesions which seem a necessary precursor of phlebothrombosis in all cases. Some very interesting work on endothelial

reactions has been done by Dr. Vincent McGovern, of Royal Prince Alfred Hospital, Sydney, and this work would seem to indicate the nature of the endothelial lesion. Briefly he has shown, both in rats and in human material, that when a vein is injured by chemical means or trauma a substance is liberated in the intima which converts a precursor of cement within the endothelial cells to argyrophilic cement granules. This substance then stimulates further production of cement granules by the endothelial cells. At the same time a metachromatic substance is produced, possibly from mast cells, which seeps through the cement lines and endothelial cells. This metachromatic substance (which may contain heparin) combines with the cement granules, causing them to coalesce as a cement film on the endothelial surface. In this way a thin gelatinous film of cement substance is poured out over the endothelium, and no thrombosis occurs. More severe grades of injury impair the production of cement and present a surface on which thrombosis frequently occurs. We can regard this imperfect formation of cement substance as an abnormal reaction of endothelium to injury. From Dr. McGovern's work it appears probable that this abnormal reaction is the endothelial lesion present in cases of phlebothrombosis. What actually constitutes the injuring factor in human material is not known. However, whatever the nature of the injuring factor, it has been found that if stasis or anoxæmia is present the reaction pattern to damage is much more likely to be abnormal. Stasis is certainly present in most cases of phlebothrombosis, and anoxæmia may be present in some cases.

With increasing age (both in the rat and in man) the endothelial reaction pattern to a fixed stimulus tends to be more commonly abnormal. This is in keeping with the increased incidence of phlebothrombosis with increasing age.

Another aspect of investigation into the endothelial defect is the investigation of the *vasa venorum*. It has been postulated that disease of the *vasa venorum* arising from the adjacent arteries may be responsible for intimal damage in the vein supplied. This is being investigated at present, but I know of no publications at present available.

In addition to the foregoing, Short has described longitudinal thickenings of the intima of the veins of the lower limbs; these, when they accompany arteries, are orientated in regard to a line joining the centre of the artery to the centre of the vein. The incidence of these thickenings of the intima increases with increasing age, and they are the usual site of attachment of thrombi in phlebothrombosis. The true nature of these thickenings is not known, but it is significant that they are the usual site of attachment of thrombi and that they increase in frequency with increased age.

From the foregoing the following may be assumed: that phlebothrombosis results from an accumulation of factors, some of which act upon the endothelium, while others act upon the circulating blood, so that no one factor can at present be considered of any more importance than another.

With regard to the actual pathology, platelets are deposited on the endothelium which has been rendered water-wettable. Contact of the platelets with this surface liberates platelet lipoid factor, also contact with this surface activates Profactor VII to form Factor VII. These two factors then start the chain of events which results in a fibrin thrombus. This thrombus retracts, liberating adsorbed thrombin, which is a very powerful autocatalyst of the coagulation mechanism, and the thrombus increases in size in the direction of blood-flow within the vein. In this way a self-propagating thrombus becomes attached to the vessel wall only at the point of origin, and often a very long thrombus is formed which may break at any point, releasing a large or small embolus. If blood flow is slow, then the thrombin released as shown above will perpetuate the thrombus. If blood flow is rapid, this thrombin is rapidly diluted and washed away and the thrombus will cease to progress. In this regard it seems that diminished rate of venous flow, which is common to all conditions in which phlebothrombosis develops, is the important factor in perpetuating the thrombus.

I must say at this point that our knowledge of the causes and mechanisms of phlebothrombosis is still primitive, and that additional factors, not mentioned above, may well be found in the near future.

Normal Mechanism of Blood Coagulation.

Basically, the generally accepted concept of blood coagulation is as follows (Macfarlane, 1955).

Blood is normally present in vessels lined by a non-water-wettable surface. When blood comes in contact with a water-wettable surface, a number of factors react to produce thromboplastin, which then converts prothrombin to thrombin in the presence of ionic calcium. Thrombin then converts fibrinogen to fibrin and a visible coagulum is seen. Thus we have the following three stages: Stage I: the formation of thromboplastin; Stage II: the conversion of prothrombin to thrombin by thromboplastin in the presence of ionic calcium; Stage III: the conversion of fibrinogen to fibrin by thrombin.

In more detail, the coagulation mechanism is as follows: On contact with a water-wettable surface, the platelets rupture and liberate a platelet lipoid factor, which combines with antihæmophilic globulin, Christmas Factor and PTA (plasma thromboplastin antecedent) in the presence of calcium ions to form an intermediate product called prothromboplastin. This substance is apparently identical with or very similar to tissue thromboplastin—for example, brain thromboplastin. Prothromboplastin is then converted by Factor VII (which is apparently the result of activation of Profactor VII by contact with a water-wettable surface) and Factor V, in the presence of calcium ions, to form thromboplastin, which then converts prothrombin to thrombin in the presence of calcium ions. Thrombin then reacts with fibrinogen, which undergoes polymerization, forming needle-shaped fibrils; these then become aligned into fibre strands, which are known as strands of fibrin. Thrombin not only acts on fibrinogen, but also has a powerful action on platelets, causing the liberation of the platelet lipoid factor and thus accelerating thromboplastin formation. This has been termed the autocatalytic reaction, and as has been pointed out above, the release of adsorbed thrombin from fibrin when fibrin retracts causes a greatly accelerated local production of thromboplastin, because of the release of lipoid factor from platelets by thrombin. This occurs especially if blood flow is slow at the surface of the thrombus, enabling a sufficient concentration of thrombin to be built up to have a significant effect on the platelets. If blood flow is rapid the thrombin is quickly washed away, and accelerated thromboplastin formation does not occur. The following two factors which inactivate thrombin occur in normal blood: (i) antithrombin (present in the albumin fraction of plasma) converts thrombin to inactive metathrombin; (ii) heparin, present in minute concentrations, will also inactivate thrombin and requires the presence of a heparin co-factor. Coagulation will occur if the rate of thrombin formation is greater than the rate of thrombin inactivation by the above-mentioned two substances.

Fibrin once formed soon undergoes retraction, and this process requires large numbers of platelets. As retraction occurs, the surface area available for adsorption of thrombin is diminished and thrombin is released into the surrounding fluid. A fibrinolysin is present in plasma, but has apparently no significant action in normal coagulation. It may be concerned in the organization and removal of intravascular thrombi.

The Site of Action of Therapeutic Anticoagulants.

Heparin is a dextrorotatory polysaccharide made up of hexosamine and hexuronic acid units containing sulphuric acid ester groups. According to Jorpes (1946), heparin, by virtue of its high sulphuric acid content, contains the strongest electric charge of any high molecular group substance in the body. The actions of heparin are as

follows: (i) it has an antithrombin action neutralizing thrombin; (ii) it reduces platelet adhesiveness—that is, it reduces the normal tendency of platelets to adhere to each other and to abnormal endothelial surfaces; (iii) heparin inactivates serotonin, which is a vasoconstrictor liberated when blood coagulates. This action may account for the dramatic relief of pain which sometimes follows the use of heparin in thromboembolic conditions. The control of heparin therapy is by the Lee and White method of estimating whole blood coagulation; this should be kept between fifteen and thirty minutes (normal range, four to ten minutes). This is a simple test to measure the coagulation of whole blood obtained by venipuncture in glass tubes of three-eighths of an inch internal diameter at 37° C. The capillary tube methods have been found quite unreliable.

The "Dicoumarin" series of drugs—dicoumarol, "Tromexan" and phenylindanedione ("Dindevan")—have a similar action. It should be noted that phenylindanedione is not related chemically to "Dicoumarol" and "Tromexan", but has a similar action to these drugs. These drugs act by depression of the level of Factor VII of the plasma, and consequently the patients treated with these drugs show very defective thromboplastin formation. Prothrombin is slightly depressed by these drugs, but the degree of depression of prothrombin is so slight that it is unlikely to contribute significantly to their anticoagulant action. The control of the drug is by Quick's one-stage prothrombin test, with the use of brain thromboplastin. No other thromboplastin should be used; for example, if Russell's viper venom thromboplastin is used the test is insensitive to changes in Factor VII and will give quite erroneous results. It will be remembered that in the coagulation of normal blood, prothromboplastin is formed which may be considered identical with brain thromboplastin. This prothromboplastin, together with Factor VII and Factor V, in the presence of calcium ions, forms thromboplastin, which converts prothrombin to thrombin, which in turn converts fibrinogen to fibrin. In the test we substitute brain thromboplastin for plasma prothromboplastin and measure the clotting time. The relationship of the patient's clotting time to the clotting time of normal plasma will record an abnormality in any of the three following reactions:

$$\text{Brain thrompoplastin} + \text{Factor VII} + \text{Factor V} + \text{Calcium} \longrightarrow \text{thromboplastin.}$$

$$\text{Prothrombin} \xrightarrow{\text{thromboplastin}} \text{thrombin.}$$

$$\text{Fibrinogen} \xrightarrow{\text{thrombin}} \text{fibrin.}$$

The Quick one-stage prothrombin test has been found to be the simplest test for accurately measuring a deficiency of Factor VII. As Factor VII is the grossly affected factor in this type of anticoagulant therapy, this method is the method of choice for control of this therapy. It is of interest that in isolated deficiency of prothrombin the result of the Quick one-stage prothrombin test may not be significantly abnormal (Biggs and Douglas, 1953).

The expression of the results of the test is very important, three methods being available: (i) a simple ratio of the patient's prothrombin time in seconds to the control's prothrombin time in seconds; (ii) a prothrombin index, which is obtained by dividing the control's prothrombin time by the patient's prothrombin time and expressing the result as a percentage; (iii) the prothrombin "concentration", which is determined as follows:

Normal plasma is diluted with saline to give serial dilutions representing 10% plasma, 20% plasma *et cetera*, up to 100% plasma. Prothrombin times are estimated on each of these serial dilutions by the Quick one-stage prothrombin test, and the prothrombin times obtained are plotted against the plasma concentration. The prothrombin time of the patient's plasma is determined, and then from the graph the dilution of normal plasma having the same prothrombin time as that of the patient is determined. This percentage dilution of normal plasma is the prothrombin "concentration" of the patient's plasma.

For any given prothrombin time the prothrombin concentration is considerably lower than the prothrombin index, and it is absolutely essential that physicians and surgeons know which percentage method has been used. For example, a prothrombin concentration of 20% is a commonly employed therapeutic level; but an index of 20% is a dangerous level of prothrombin depression.

Of the three methods of expressing results the simple ratio or the prothrombin index is to be preferred to the prothrombin concentration, for the following reasons: (i) They are simpler and there is less chance of error in calculating the results. (ii) The prothrombin concentration has an additional error in the error of the calibration curve of dilutions of normal plasma. (iii) The calibration curve required for the prothrombin concentration is often not calculated, a calibration curve from a monograph being used; this no doubt must differ from that curve obtained in the laboratory where the test is being carried out, because of variations in activity of the batches of reagents used.

The therapeutic level of "prothrombin" to be aimed at is as follows: (i) a prothrombin time two or three times normal; (ii) a prothrombin index of 33% to 50%; (iii) a prothrombin concentration of 10% to 30%. Levels below these may give rise to hæmorrhage, hæmaturia being the commonest manifestation. Hæmorrhage sometimes occurs at the foregoing therapeutic levels, but is rare.

A further action of the "Dicoumarin" series of drugs is that, like heparin, they reduce platelet adhesiveness.

The antagonist of these drugs is vitamin K_1 oxide; this when given orally or intravenously will restore the result of the Quick one-stage prothrombin test to normal within twelve hours. It is of interest that one theory of the action of dicoumarol-like compounds is that they replace vitamin K in enzyme systems necessary for the formation of Factor VII and prothrombin in the liver. It is significant in this regard that the coagulation defect produced by vitamin K deficiency is indistinguishable from that produced by the "Dicoumarin" series of drugs.

Rationale for the Use of Anticoagulants in Thrombosis.

In experimental animals it has been shown by various groups of workers that heparin or dicoumarol will prevent the formation of thrombi in veins which have been mechanically or chemically damaged. Of course, if the degree of trauma or chemical irritation exceeds a certain level, thrombi will occur despite the anticoagulants; but in these cases the thrombi are certainly less extensive in treated than in untreated animals.

Solandt and Best (1938), working with experimental animals in which sodium ricinoleate solution was kept in contact with the coronary artery endothelium for five minutes, showed that thrombosis of the coronary artery occurred which could be prevented by heparin.

Solandt, Nassim and Best (1939) produced mural thrombi of the left ventricle of animals by subendocardial injections of sodium ricinoleate solution. These mural thrombi could be prevented by heparin.

In myocardial infarction produced by the ligation of coronary arteries in dogs, anticoagulants have no effect on the course of the disease.

Whilst the foregoing experimental evidence gives some support to the use of anticoagulants in thromboembolic diseases, it must be realized that it is quite impossible to produce conditions in experimental animals which resemble, for example, coronary atheroma complicated by myocardial infarction, or phlebothrombosis. Thus the answer to the efficacy of anticoagulants must lie in the observation of large, carefully controlled series of patients treated with these drugs. Dr. E. J. Halliday will deal with the results of such series.

Tests Alleged to Indicate Thrombosis.

As it would be of tremendous clinical value if laboratory tests could reveal the presence of a thrombotic state, I will discuss certain of these tests.

Fibrinogen may be clotted, not only by thrombin, but also by papain, chloramine T, ninhydrin and potassium 1,4 naphthoquinone 2 sulphonate. Cummine and Lyons (1948) found that certain samples of plasma were clotted by naphthoquinone, and from their investigations concluded that the fibrinogen clotted by naphthoquinone was not normal fibrinogen, but fibrinogen B. Also they found that the presence of fibrinogen B together with a shortened capillary tube coagulation time indicated a prethrombotic or thrombotic state. Other coagulation workers have not been able to confirm these findings. In addition, the capillary tube coagulation method has been shown to be unreliable.

The following are some changes in the blood which have been reported to be present in patients suffering from thrombosis: (i) diminished antithrombin level; (ii) reduction in the number of platelets immediately before the clinical onset of thrombosis; (iii) shortening of the coagulation time in lustroid tubes; (iv) shortening of the coagulation time in siliconed tubes.

The last two findings suggest that some change in the coagulation mechanism is associated with thrombosis; but unfortunately a standard technique with these tubes is difficult to develop, and the tests could hardly be used in the routine laboratory.

At present there are no tests for the detection of blood changes which may precede or accompany thrombosis. The reason for this is that thrombosis is probably the result of a concentration of adverse circumstances rather than the result of any one specific abnormality of the blood.

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SOME GEOGRAPHICAL ASPECTS OF THE MORTALITY FROM MELANOMA IN EUROPEANS.

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THIS paper considers the possibility that the incidence of melanoma of the skin is dependent on some geographical or climatic feature. The mortality statistics from as many countries as possible have been examined to determine the variations in the incidence of melanoma as measured by mortality throughout the world. As the fair races differ from the dark-skinned races in their reaction to sunlight and in the incidence of melanoma, the study has been confined to the relatively fair-skinned types, who may be collectively referred to as Europeans. Melanoma is used throughout in the sense of "malignant melanoma". It is shown that the distribution of melanoma is consistent with the hypothesis that excess of sunlight is an important predisposing cause of melanoma. A second paper will deal with a clinical survey of patients with melanoma in Australia, designed to compare exposure to the sun of melanoma patients with that of controls.

Melanoma in Australia.

Melanoma has had a separate rubric in the "International List of Causes of Death" only since the sixth revision, which was adopted by most countries in about 1950. Prior to this deaths due to melanoma were classified under malignant tumours of the skin or under malignant tumours of the particular organs in which they occurred. However, Australian statistics on deaths from melanoma are available for the years since 1930 in *Demography*, the annual bulletin of the Bureau of Census and Statistics, Canberra, not in the main table of deaths, but in a supplementary classification of the cancer deaths according to cell type. I have already commented on the figures for the years 1931 to 1940 (Lancaster, 1954). I also noted that in 1951 the crude death rate from melanoma in Australia was about two and a half times the crude death rate from melanoma in England and Wales. A similar comparison is made graphically in Figure I, where the death rates from melanoma in Australia in the years 1951 to 1953 are compared with those of England and Wales in the years 1950 to 1953. It was suggested that sunlight

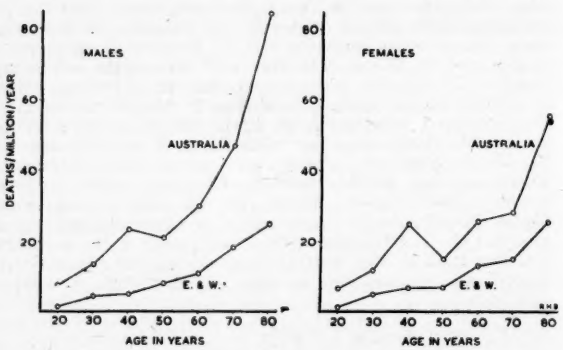

FIGURE I.

A comparison of the mortality from melanoma in Australia, 1951 to 1953, with that in England and Wales, 1950 to 1953. The upper curves are the Australian.

was probably an important factor. This suggestion had originally been made by McGovern (1952), on the basis of pronounced differences between his series and other series from England and overseas in site and in the ages of patients.

In Table I are given the death rates from melanoma for Australia in four periods over the years 1931 to 1953. For any given period and age the male rates are usually higher than the female rates. In both sexes the death rates increase with age, but not nearly so rapidly as do the rates for other cancers. For example, in the period from 1951 to 1953 the death rates at ages sixty-five to seventy-four years are less than four times the death rates at ages twenty-five to thirty-four years. This low rate of increase with age is quite unusual among the cancers. If attention is now fixed on any age group, there has been an increase in the Australian death rates, even though the deaths from melanoma in the period from 1951 to 1953 are restricted to those from melanoma of the skin (rubric 190 of the International List, sixth revision), whereas in the previous periods melanoma of any site was included in the special tabulations for melanoma.

Dr. A. G. S. Cooper, of the Queensland Radium Institute, Brisbane, has believed for some years that sunlight is an important predisposing factor in melanoma, and that melanoma is more common in the northern parts of

TABLE I.

The Mortality from Melanoma in Australia.

Ages (Years).	Deaths per Million *per Annum*.							
	1931 to 1940.		1941 to 1945.		1946 to 1950.		1951 to 1953.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
0 to 14	0	0	0	0	0	0	0	1
15 to 24	3	2	3	3	3	2	8	7
25 to 34	7	6	10	5	11	11	12	12
35 to 44	8	6	9	12	16	17	23	25
45 to 54	13	12	15	14	22	16	21	15
55 to 64	22	14	20	23	30	20	30	26
65 to 74	28	19	17	23	36	24	47	28
75 and over	34	33	28	36	60	53	84	56
All ages ..	8	6	8	9	13	11	16	13
All ages, both sexes	7		9		12		14	

Queensland than in the southern, which is also true for rodent ulcer and epithelioma. Table II tests a similar hypothesis for the States of Australia. The centre of gravity of the population in each State is not far from the capital city, because a large proportion of the population lives in the capital city or in districts near by. The

TABLE II.

State.	Latitude (South) of Its Capital.	Melanoma Deaths per Million.		
		Males.	Females.	Persons.
Queensland	27	28	17	23
Western Australia ..	32	13	17	15
New South Wales ..	34	17	13	15
South Australia	35	15	10	12
Victoria	38	8	8	8
Tasmania	43	7	9	8
Australia	35	16	12	14

only exception is Queensland, in which there are some large aggregations of population in the north at a distance from the capital, so that the centre of population may be a degree or so north of the capital. It is therefore reasonable to take the latitude of the capital city as a good approximation to the latitude of the centre of population. A gradient in the death rates due to melanoma is evident as the States are ordered from north to south, and the crude death rates due to melanoma in Queensland are almost three times those in Tasmania and in Victoria.

In the next few sections the experiences of other countries are given for comparison with the Australian experience. However, a glance at an atlas will show that no other country in either hemisphere has a large number of persons of relatively pure European extraction living in the tropics and in a temperate zone as well. Moreover, the system of vital statistics is not sufficiently developed in some countries to enable comparisons to be made. It will be evident later that although Canada and the United States or Europe itself can yield just as big a stretch of latitude, the gradient in the mortality at these higher latitudes is not so pronounced as in Australia.

Melanoma in New Zealand.

Eastcott (1954) noted in his report for the British Empire Cancer Campaign that melanoma was more common in New Zealand than in England and Wales, and gave a table (his Table CXIV) of rates by age and sex for the deaths from melanoma. Later, he (Eastcott, personal communication, 1955) supplied me with the deaths by age and sex for the two islands of New Zealand. The centre of the population in North Island has approximately the same latitude as Sydney, the centre in the South Island the same as Melbourne. The rates are given in Table III for the two islands separately and for New Zealand as a whole. As there is only one medical school and one bureau dealing with vital statistics in New Zealand, the criticism cannot be made that the differences are due to different training or different statistical practices. On the other hand, the total population of New Zealand is small, and so the sampling errors, as measured by the coefficient of variation, will be large. With this in mind we note that the death rates in the North Island are in general higher than those in the South Island. In both islands the rates in young adult life, ages twenty-five to thirty-four years, are high, as they are in Australia also, compared with rates at the same ages in England and Wales.

Melanoma in the British Isles.

The melanoma death rates in the British Isles are of especial interest, as Australia and New Zealand have been largely colonized from Britain. The Eire figures have been computed from tables sent by Dr. R. C. Geary (personal communication, 1955). The figures for Scotland and for England and Wales have been computed from the annual reports of the two registrars-general.

A graphical comparison between the rates in Australia and in England and Wales has already been given in Figure I. The death rates by age are given for England and Wales, for Scotland and for Eire in Table IV. In these countries the rates are much lower than in Australia, especially over the years of young adult life. Now fairness of skin is often given as an important predisposing cause of melanoma, for example by Raven (1953), but we can see that the populations of Scotland and Eire suffer from this disease much less than the population of Australia. It seems that a climatic factor is necessary to explain the difference. I have suggested that a hopeful line of research would be to follow up those Scottish or English troops who have had tropical service and returned to live again in Scotland or in England (Lancaster, 1955).

Melanoma in Other European Countries.

Melanoma is numerically unimportant in Europe, and often the deaths under rubric 190 of the "International List of Causes of Death" are not listed separately. Because of this and of the unavailability of the annual reports of the European countries in Sydney, I have written to the official statisticians of a number of the countries and summarize their replies in Table V. It is evident that melanoma is certified as a cause of death much less commonly in Europe than in Australia and New Zealand. In Norway, however, the rates are higher than in the other European countries. Dr. Julie Backer (personal communication, 1955) considers that the figure is perhaps 50% higher than it would otherwise be because, under the close cooperation between the Norwegian Cancer Registry and the Bureau of Statistics, questions are sent

TABLE III.

The Mortality from Melanoma in New Zealand.

Ages (Years).	Deaths per Million *per Annum*.							
	New Zealand. (1949 to 1953).		North Island. (1943 to 1953).		South Island. (1943 to 1953).		New Zealand. (1943 to 1953).	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
0 to 14	0	0	1	0	0	0	0	0
15 to 24	5	10	6	9	2	2	5	7
25 to 34	15	12	8	10	13	4	10	8
35 to 44	17	11	17	14	11	5	15	11
45 to 54	31	28	29	17	17	19	25	18
55 to 64	21	10	34	24	7	13	24	20
65 to 74	30	35	33	35	32	13	33	27
75 and over	50	28	54	30	47	39	51	33
All ages	14	12	14	12	10	7	13	10
Both sexes	13		13		8		12	

to doctors to elucidate imprecise death certificates. The rates from Sweden are also high, relative to those of the other European countries. On the other hand, the rates from France, which do not rise above three deaths per million *per annum* in any age group, are strikingly low. In Italy, too, the rates are low. It is probable that local differences in medical certification and statistical coding practices are responsible for the unexpected variation between the rates in these European countries. It will be of interest to reconsider the rates after some years, as the sixth revision of the International List has made a great departure from previous revisions by giving melanoma a separate rubric.

TABLE IV.

Mortality from Melanoma in the British Isles.

Ages. (Years.)	Deaths per Million *per Annum*.					
	Eire. (1950 to 1954.)		Scotland. (1950 to 1953.)		England and Wales. (1950 to 1953.)	
	Males.	Females.	Males.	Females.	Males.	Females.
0 to 14 ..	0	0	0	0	0	0
15 to 24 ..	0	0	0	0	1	1
25 to 34 ..	1	1	1	3	4	5
35 to 44 ..	4	3	5	5	5	7
45 to 54 ..	4	6	9	8	8	7
55 to 64 ..	5	3	9	8	11	13
65 to 74 ..	14	2	17	5	18	15
75 and over ..	4	25	29	18	25	26
All ages ..	3	3	5	4	6	7
Both sexes	3		4		6	

Melanoma in the United States of America.

The United States Bureau of the Census has supplied me with a tabulation of the deaths from melanoma over the years from 1949 to 1952, classified by age, sex, race and State. I have used the deaths of only the white population in each State. The concept of race used by the Bureau is derived from that which is commonly accepted by the general public (United States Census of Population, 1950). The non-whites are Negroes, Indians, Japanese, Chinese and "other non-white races". Persons of Mexican birth, who were not definitely of Indian or other non-white race, were classified as white. "Negro" includes persons of mixed white and non-white parentage.

For our purposes none of the common subdivisions of the Bureau are adequate; but I have attempted whenever possible to follow the groupings of the States, to which the Bureau refers as "divisions". The aim of my groupings is to give comparisons between north and south and coastal and inland areas. I have used the 40th parallel as a guide to the dividing line between northern and southern groups.

I have grouped the States into areas, indicated graphically in Figure II, as follows: (i) A North Pacific Area consisting of Washington and Oregon. (ii) A North Mountain Area, consisting of the northern States of the "Mountain Division" of the Bureau — namely, Montana, Idaho and Wyoming. (iii) A North Central Area, consisting of the West North Central and East North Central Divisions of the Bureau. In detail this area confines the States of North and South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Wisconsin, Michigan, Illinois, Indiana and Ohio. (iv) A North-East Area consisting of Pennsylvania, New Jersey and all States to the north with an Atlantic seaboard. (v) California, the South Pacific Area. (vi) A South Mountain Area, consisting of Nevada, Utah, Colorado, Arizona and New Mexico. (vii) A South Central Area, consisting of Arkansas, Oklahoma,

TABLE V.

The Mortality[1] from Melanoma in Some European Countries.

Ages (Years).	France (1952 and 1953).		Italy (1951 to 1953).	Switzerland (1951 to 1953).		Netherlands (1951 to 1954).		Norway (1951 to 1953).		Sweden (1952 and 1953).	
	Males.	Females.	Both Sexes.	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
15 to 24	0	0	0	2	1	0	1	2	0	1	1
25 to 34	0	0	1	3	4	4	2	6	4	3	2
35 to 44	0	1	2	10	5	4	5	7	7	11	9
45 to 54	2	2	3	4	6	8	7	15	17	11	11
55 to 64	2	1	5	23	12	12	10	20	18	20	14
65 to 74	2	2	6	19	11	27	24	36	42	43	19
75 and over	3	3	10	17	23	15	17	45	34	43	32
All ages	1	1	2	7	5	5	5	9	10	10	8

[1] Deaths per million *per annum*.

TABLE VI.

The Mortality from Melanoma in the United States.[1]

Area.	Sex.	Deaths per Million *per Annum* at Ages (Years).							
		15 to 24.	25 to 34.	35 to 44.	45 to 54.	55 to 64.	65 to 74.	75 and Over.	All Ages.
(1) Oregon and Washington	M.	2	10	5	16	20	35	34	9
(2) North Mountain	M.	2	5	5	12	22	33	47	8
(3) North Central	M.	2	5	9	15	23	28	46	9
(4) North East	M.	3	8	12	16	21	31	45	10
(5) California	M.	4	8	20	25	34	39	64	15
(6) South Mountain	M.	1	5	8	9	26	21	61	7
(7) South Central	M.	4	9	16	21	34	48	62	13
(8) South Atlantic	M.	2	9	13	23	28	30	50	11
(1) Oregon and Washington	F.	2	9	6	13	13	24	33	8
(2) North Mountain	F.	2	2	8	29	17	29	67	9
(3) North Central	F.	2	4	9	14	17	23	35	8
(4) North East	F.	2	5	9	11	19	20	30	8
(5) California	F.	3	8	15	15	16	28	61	11
(6) South Mountain	F.	1	6	10	10	16	38	64	8
(7) South Central	F.	3	9	11	19	26	35	54	10
(8) South Atlantic	F.	3	6	9	17	20	27	45	9
United States	M.	3	7	12	17	25	33	49	11
United States	F.	2	6	10	14	19	25	40	9

[1] See text and Figure I for the definition of the areas.

Louisiana, Texas, Kentucky, Tennessee, Alabama and Mississippi. (viii) The South-East Area, consisting of West Virginia, Maryland, Delaware and other States to the south with an Atlantic seaboard. (See Figure II). In Table VI, I have given the death rates by age and sex for these areas or groups of States. The general conclusions are that the rates are somewhat higher in the southern areas than in the northern, and that the seaboard groups of States have a higher mortality than the mountain or central. This feature is repeated in the South African figures. Since the Australian and New Zealand populations are both almost entirely coastal, no other comparisons between persons living on the seaboard and those inland is possible among the populations considered. In South Africa the Natal and Cape crude rates are higher than the Transvaal rates, although Transvaal is more northerly—that is, has a lower latitude. A plausible explanation appears to be that surfing and swimming lead to greater exposure in the coastal areas.

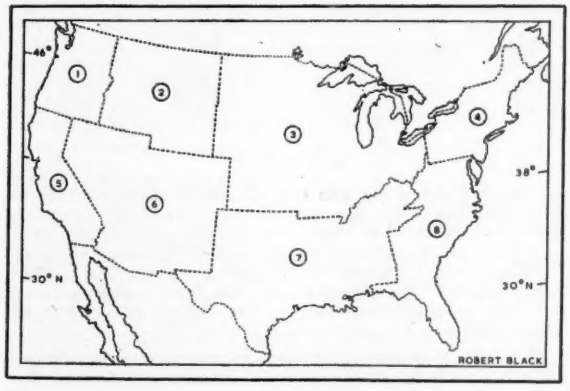

FIGURE II.

The areas chosen for comparison in the United States. See text for an enumeration of the States included in each area.

The United States death rates as discussed above do not give as striking a contrast as the incidence of morbidity rates. Dorn and Cutler (1954) report a survey of cancer morbidity in the United States carried out for the National Cancer Institute. They give comparisons for three groups of States, which they term West, North and South. West comprises the first, second, fifth and sixth areas of Figure II, North the third and fourth areas, and South the seventh and eighth areas. They give the following incidence rates per million for melanoma of the skin: North, 13; South, 39; West, 33; and the corresponding figures for carcinoma of the skin, 292, 1133 and 785. Thus melanoma of the skin tends to have the same geographical distribution as carcinoma of the skin. The population in their West is concentrated largely in California, and so is at a lower latitude than that of the North. These morbidity figures are obviously more striking than the mortality figures, and this effect is to be noted also in Australia. A large hospital in Sydney will have, say, 40 new cases of melanoma per year, whereas in Melbourne a hospital of comparable size will have about 12. Detailed consideration is best deferred to a later paper, after the clinical survey of melanoma in Australia has been completed.

Melanoma in Canada.

In Table VII are given the death rates from melanoma in Canada, computed from data supplied to me by the Canadian Dominion Bureau of Statistics. These figures are of interest chiefly because the rates are much lower in Canada than in the United States. However, such comparisons are of less value than those made within a single country.

Melanoma in South Africa.

In Table VII are also given the mortality rates from melanoma in the white population of South Africa, computed from data supplied to me by Dr. H. M. Stoker, Director of the Office of Census and Statistics. Dr. Stoker (personal communication, 1955) points out that the crude death rates per million *per annum* for both sexes combined are as follows: Natal, 18; Cape of Good Hope, 13; Transvaal and Orange Free State, 10; with an average of 12 for the whole Union over the years from 1949 to 1952. The most northerly provinces, Transvaal and Orange Free State, had the lowest rates. It is possible that these figures are best explained by noting that Natal and the Cape both have populations living in easy distance of the sea, whereas Orange Free State and Transvaal are inland.

The Effect of Climate.

Although we have at this stage no direct evidence that sunlight is the factor responsible for the variations in the incidence of melanoma throughout the world, we may

consider now the intensity of the biologically active light throughout the world.

The sun radiates electromagnetic energy over a wide band of frequency or wave-length as if it were a hot, dark body at a temperature of about 5800° K.—that is, 5800° on the absolute temperature scale. However, only recently (Tousey, 1953) has it been possible, by means of rockets carrying spectrophotometers, to obtain measurements of the intensity of the shorter wave-lengths.

The intensity of sunlight is usually measured as that falling on a unit horizontal area. Without absorption by the atmosphere the intensity would be given by the formula

$$I_\psi = I_0 \text{ Cos } \psi \text{ —— (1),}$$

where I_0 is the intensity when the sun is at the zenith and ψ is the angle between the direction of sun and the vertical. However, the existence of an atmosphere brings modifications to this formula in several ways.

First, ozone has an absorption band in the ultra-violet end of the spectrum. It may be taken that the ozone in the atmosphere is equivalent to a layer of ozone a quarter of a centimetre thick at normal temperature and pressure, and that most of the ozone is at great heights—the average height of the ozone is perhaps 22 kilometres (Mitra, 1947). Now the absorptive effect of this layer will be greatly enhanced if the sun is not near the zenith, for the effective thickness with the sun at an angle of ψ from the zenith will be proportional to the secant—that is, the reciprocal of the cosine of ψ. This is of great importance, because the logarithm of the intensity of light received after passing through an absorptive layer is equal to the logarithm of the initial intensity less a constant number of times the thickness. The practical effect of this is that little ultra-violet light is received directly from the sun when it is more than about 45° from the zenith. Second, there is scattering of light by the molecules of the air and by fine particles. The amount of scattering is proportional to the fourth power of the frequency, so that the light of the ultra-violet end of the spectrum undergoes more scattering than the red. The blue colour of the sky is, indeed, due to this effect. The scattering effect enables some ultra-violet light to pass through the ozone layer vertically or nearly so, and hence complete absorption does not occur even when the sun is low. Indeed, graphs can be drawn, as in Luckiesh (1945), showing the amount of ultra-violet light received on a horizontal surface from the sun directly and from the sky for varying heights of the sun. This radiation from the sky is well known to surfers, who may receive an erythema dose without having been directly exposed to much of the direct radiation of the sun. Third, dust in the atmosphere may also absorb ultra-violet light; this is usually unimportant. Fourth, heavy cloud may absorb or reflect upwards much ultra-violet light; but, in general, countries with wet climates do not receive much less ultra-violet light than those with dry climates.

It would be of great interest to be able to give the total amount of ultra-violet light incident on the various countries of the world. In the past, chemical methods have been used; but Koller (1952) believes that the chemical methods can be carried out with accuracy only under the strictest experimental conditions. He finds that the best chemical method is the decomposition of oxalic acid in the presence of uranyl sulphate, a method used for the only Australian observations we know of (Clements and Golding, 1936). However, this method measures longer wave-lengths—3132 to 4100 Ångström units—than are of interest to us here. It appears that only electrophotometric methods are of sufficient accuracy in the ultra-violet zone of the spectrum (Koller, 1952). These methods are difficult and expensive to carry out.

TABLE VII.

The Mortality from Melanoma in Canada and South Africa.

Age. (Years.)	Deaths from Melanoma per Million *per Annum*.			
	Canada (1950 to 1953).		South Africa (White Population) (1949 to 1952).	
	Males.	Females.	Males.	Females.
0 to 14 ..	0	0	0	0
15 to 24 ..	1	1	7	4
25 to 34 ..	4	4	8	9
35 to 44 ..	6	5	17	12
45 to 54 ..	9	7	14	20
55 to 64 ..	13	10	46	8
65 to 74 ..	17	15	67	21
75 and over ..	17	21	142	137
All ages	5	4	15	10

TABLE VIII.

Mortality of Melanoma by Country and Latitude.

Country or Geographical Area.	Latitude of Centre of Population.	Deaths from Melanoma per Million *per Annum*.
South Island, New Zealand	45° S.	8
North Island, New Zealand	39° S.	12
Victoria	38° S.	8
New South Wales	34° S.	15
Cape of Good Hope, South Africa ..	32° S.	13
Natal	29° S.	18
Transvaal and Orange Free State ..	27° S.	10
Queensland	27° S.	23
California, United States of America ..	37° N.	12
North East, United States of America	42° N.	9
Italy	43° N.	2
Switzerland	47° N.	6
France	48° N.	1
Canada	50° N.	5
Netherlands	52° N.	5
England	53° N.	6
Eire	53° N.	3
Scotland	56° N.	4
Sweden	59° N.	9
Norway	61° N.	10

Discussion and Summary.

A case has been made above for the hypothesis that the incidence of melanoma varies with latitude and is commoner as the tropics are approached, the crude death rates from melanoma being given in Table VIII. It is understood that throughout only populations of European descent are being considered. It has seemed natural to link this effect with the variation in ultra-violet radiation with latitude, as has been done in the case of the skin carcinomata. Subsidiary factors will be customs affecting dress and sport, especially swimming and surfing. That swimming may be of importance has been noted above in the discussion of melanoma in the United States and in South Africa.

However, it appears that some of the variations between countries may be due to varying practices of certification and statistical classification, although it is rather surprising that a cutaneous cancer with the distinctive clinical features of melanoma should not be almost invariably diagnosed as such in those who die of the disease. The instructions of the sixth revision of the "International List of Causes of Death" are sufficiently precise; but, owing to its relatively small numerical importance, melanoma tends to be lumped together with a number of miscellaneous tumours into some composite rubric such as "malignant tumours of other organs". Moreover, melanoma has been classified separately only for the few years since 1950.

An enumeration of the cases within certain areas would be of value, but as a rule this can be done only if a cancer registry has been established. A clinical survey under the ægis of the New South Wales Cancer Council is being carried out at the present time and will be reported in a second paper.

The early Australian workers in the skin cancers, for example, N. Paul (1918) and E. H. Molesworth (1927, 1944), were greatly impressed by the high frequency of skin cancer in Australia, and had no difficulty in relating the high incidence of rodent ulcer and epithelioma to the solar radiation. However, neither appears to have given attention to the possibility that solar radiation might also cause a high incidence of melanoma. Nor do the textbooks assign any importance to this factor. Many textbooks have been examined on this point, but in none has an explicit suggestion been found. In fact, the discussion of the ætiology is usually made secondary to a comparison of the rival views on ontogenesis. Brief mention is usually made of the importance of skin colour, the fair being more susceptible, and then the importance of trauma by unskilful removal of moles is stressed. It seems probable that skin colour is of importance because fair skins allow the harmful radiations to penetrate to susceptible cells.

The earliest explicit mention of the importance of exposure to the sun that I have found is that of McGovern (1952), although it would not cause surprise if an earlier mention was to be found, since it appears that some clinicians—for example, A. G. S. Cooper—have held this view for some years. Moreover, one might expect on prior grounds that the induction of cancer in a cell might be related to its functional activity.

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THE MECHANISM OF FLUID RETENTION IN HEART FAILURE.

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ONE of the essential features of heart failure is an abnormal tendency to retain fluid, with development of a state of hyperhydration. So characteristic is this of heart failure that explanations of the mechanism of failure are largely concerned with how fluid retention may occur. Thus Starling's "back pressure" theory postulated a piling up of blood in the venous system under high pressure behind the failing heart pump. This rise in venous pressure leads to loss of fluid from the vessels due to upset of capillary equilibrium, and the resultant hæmoconcentration leads to retention of salt and water by the kidneys. The fundamental assumption of the Starling theory was that the venous pressure would rise as a direct mechanical effect of the heart failing to pump some hypothetical amount of blood, and that therefore the height of the venous pressure was an indication of the strength or weakness of the heart. This presumes some force maintaining venous return independent of cardiac output; no such force has been demonstrated. Starr (1949) found, working on dogs, that maximal destruction of the right ventricle caused no rise in venous pressure unless there was a prior increase in blood volume. Exercise, however, caused a marked increase of venous pressure which was not sustained when the animal was again at rest. Starr measured the venous pressure in patients with congestive failure immediately after death, and found that the main increment of the pressure during life was still present. Thus an increase in static pressure, which can be due only to an increase in blood volume, accounts for the major part of the increased venous pressure in congestive heart failure.

The following other facts inconsistent with the back pressure theory are found in recent experimental work.

1. The blood volume is increased and there is hæmodilution instead of hæmoconcentration, which should be present if there was a primary increase of venous pressure with loss of fluid from the capillaries. Similarly, Warren and Stead (1944) precipitated congestive failure in two compensated cardiac patients by giving salt and withholding diuretics, and demonstrated an increase in blood volume and hæmodilution, with a gain in weight before any significant rise in venous pressure developed.

2. When congestive failure occurs in association with anæmia, Paget's disease, anoxic pulmonary disease, thyrotoxicosis, beriberi or an arterio-venous aneurysm, the cardiac output may be found to be well above normal, and when the associated abnormal condition is cured the patient's heart function may appear to be normal.

3. Brod and Fejfar (1950), in detailed studies on ten patients with moderately severe congestive failure, who had a spontaneous diuresis at night, found that changes in the urine flow were not preceded by any consistent change in the right auricular pressure. After such changes in flow the changes in the right auricular pressure were more consistent, the pressure tending to rise as the output of urine declined and vice versa.

It seems, then, beyond doubt that we must abandon the idea that a rise in venous pressure is the primary event in the pathogenesis of fluid retention in congestive cardiac failure. Similarly, prerenal deviation of fluid by other means cannot account for the facts and, in addition, if increased capillary permeability or lymphatic obstruction was involved, the œdema fluid would be rich in protein, but in congestive failure it is not. The plasma protein concentration is often slightly lowered, but not usually so much as to be an important factor in œdema formation.

The most likely train of events is that the failing heart is unable to pump enough blood to meet tissue demands, as a result of which some substance or substances are

produced which, acting on the kidney, cause salt and water retention; or, on the other hand, this inadequacy of blood supply may affect kidney function directly, by reducing the renal plasma flow and the glomerular filtrate. The heart output thus may be relatively or absolutely decreased, and when there is present some condition (such as thyrotoxicosis) which greatly increases the demand of tissues for blood, it is not remarkable that output is greater than normal even in the presence of congestive failure. When there is diminished cardiac reserve the output may be quite adequate at rest but may fail to increase with activity in proportion to demand. Thus one of the earliest indications of heart failure is the development of œdema during the day, with excretion of the retained fluid during the night, when heart output is sufficient to meet the smaller tissue needs. Only when there is heart failure at rest can one expect to find a reduction in output at rest, and Merrill's patients, who developed œdema when receiving a ward diet at bed rest, uniformly had a low cardiac output.

How the kidney is involved in the development of œdema is still highly controversial. Merrill, Warren, Stead, Brod and Fejfar consider that the main factor is a reduction of renal blood flow. Their experimental work suggests that whenever cardiac output is inadequate to meet tissue needs there is an emergency redistribution of blood in which the kidneys suffer disproportionately; for when cardiac output is halved renal blood flow may be reduced to as little as one-fifth. Since the kidneys normally may have 20% to 25% of the total cardiac output, this renal shut-down mechanism can divert very useful amounts of blood to other tissues. According to Merrill, all is well until the renal plasma flow falls below 200 millilitres per minute or the critical filtration rate of about 70 millilitres per minute is reached. At higher rates of renal plasma flow the filtration rate remains within normal limits, owing to an increase in the filtration fraction. Efferent arteriolar spasm is consistent with a high filtration fraction because it increases the pressure in the glomerular capillaries. Thus Merrill considers that renal shut-down is due to efferent arteriolar spasm produced by renin, and claims to have shown that there is an increased concentration of renin in the renal venous blood in patients with congestive failure. However, renin produced by the kidneys cannot account for the diversion of blood to meet increased tissue needs, and it would seem that some other substance, produced by ischæmic or anoxic tissue, is required to explain renal shut-down, which persists only for so long as the blood supply to such tissue is inadequate.

On this hypothesis, retention of salt is due to the critically reduced filtration rate, whilst tubular function remains approximately normal. The tubules do reabsorb a greater percentage of the filtered load of salt and water; but because of the reduced amount of filtrate the total quantity reabsorbed is much less than normal. Other workers doubt that this alteration in renal hæmodynamics is sufficient to explain chronic sodium retention, and have found that clinical improvement with increased salt excretion and loss of œdema may occur without any rise in the depressed glomerular filtration rate. Because of a lack of correlation between salt excretion and filtration rate, greater emphasis has been placed on increased tubular reabsorption in the production of sodium retention.

These criticisms have been answered by pointing out that estimations of renal blood flow performed when the patient is at rest are significant only when there is heart failure at rest. In some cases the technique has been at fault, for the possibility of error when the inulin method is used to determine filtration rate is large, and this method used alone is not considered satisfactory. The detailed work of Brod and Fejfar answers other objections and illustrates very clearly the relation between the changing pattern of renal blood flow and spontaneous diuresis in patients with congestive failure. Brod and Fejfar studied 35 patients, 10 of whom were in normal health or else suffering from only trivial complaints; the remaining 25 had heart disease, and 19 had varying degrees of heart failure. Ten of the patients with heart failure had a nocturnal diuresis associated with changes which differed considerably from those observed in the other patients, whose urine flow either did not change or declined at night. Thus the renal blood flow in patients with heart failure was very low, but invariably increased when the urine flow increased and declined with a diminution of urine. Likewise changes in glomerular filtration ran parallel with changes in urine flow (both in normal and in cardiac subjects), but accounted for only a small portion of the total diuretic change. The greater portion was due to a decrease in tubular reabsorption of water. Because of the striking time coincidence of the increase in renal plasma flow and the fall in tubular reabsorption of water, this effect was not attributed to inhibition of the posterior pituitary lobe, but to a small increase in the paraglomerular blood flow. (Apparently a very small increase in the paraglomerular blood flow greatly reduces tubular reabsorption.) The increase in renal blood flow took place without a change in cardiac output, and was attributed to a return of blood to the kidneys during the period of rest. When heart failure is more severe, so that tissue anoxia continues even during complete rest at night, blood remains shunted from the kidneys and the tendency to retain salt and water remains a permanent feature.

Brod and Fejfar have done further work on the excretion of chlorides in heart failure on the same group of patients. As a result they conclude that the very low output of chlorides and possibly of sodium is due to diminished tubular chloride and sodium load, with an almost complete reabsorption of these electrolytes made possible by a low urine flow. On the other hand, they suggest that the increase in chloride excretion in cardiac patients during nocturia is produced by diminished distal tubular chloride reabsorption, due to a shorter time when the chloride is in contact with the tubular cells.

No matter how well the mechanics of renal function and altered renal hæmodynamics have been related to the abnormal salt and water balance of patients with heart failure, there remain workers who consider that these mechanisms are inadequate to account for the facts, and cite particular experiments to illustrate their criticisms. Often these are acute experiments performed in animals, which may well produce results which have no parallel with chronic heart failure in man. Such applies to the experiments on dogs quoted by Barger, Rudolph and Yates (1954), in which the functional capacity of the kidney for sodium excretion was tested by an intravenous sodium load in normal dogs and in dogs with extremely mild right-sided valvular lesions. After saline infusion, glomerular filtration rate and renal blood flow were found to rise to the same extent in both groups, but the excretion of salt and water in the dogs with mild valvular damage was less owing to increased tubular reabsorption. Since digitoxin restored normal sodium excretion in the dogs with valvular damage, it seems likely that the effects were directly related to reduced cardiac reserve in these animals. The cardiac output probably did not rise so high as in normals, and there may have been a transient increase in venous pressure. Any increase in venous pressure is a stimulus to increased tubular reabsorption of sodium, but the effect does not last. Thus ligation of the inferior *vena cava* above the renal veins causes a reduction in renal blood flow, glomerular filtration rate and sodium excretion; but though the renal venous pressure remains high, within a week these values are approaching normal.

It seems that a raised venous pressure due to obstruction of any major vein leads regularly to decreased sodium and water excretion, though renal plasma flow and glomerular filtration rate remain unchanged. Rice *et alii* (1952), in a study of a patient with spontaneous thrombosis of the superior *vena cava*, were able to demonstrate that the liability to œdema was not limited to the area of increased venous pressure; for whereas facial œdema was present on waking in the morning, pronounced œdema of the feet occurred during the day when the patient was out of bed. Having shown an impaired ability to excrete an oral salt load, they concluded that increase in reabsorption of sodium paralleled the venous congestion and was

the cause of it. Since the rise in venous pressure persisted (and was probably permanent) after the tendency to œdema had disappeared, some factor other than the rise in venous pressure was the cause of the altered fluid balance. It may be that the essential feature is impaired blood flow through the tissues with tissue anoxia; this would be temporary, as the circulation gradually improves.

In some patients with heart failure salt is retained not only by the kidneys, but also by the sweat glands and the colon. To account for this an increased secretion of suprarenal corticoids has been suggested, for it is known that the sweat sodium content is low in Cushing's syndrome. However, Merrill found that the sweat sodium content was reduced only in patients with advanced heart failure; those in whom failure was less severe had a normal sweat sodium concentration. Equally controversial is the demonstration of increased antidiuretic activity of the urine; other workers have not been able to repeat these results.

In the normal subject there is a decline in salt and water excretion in the standing position, and the factors responsible for this have been investigated by Lombardo *et alii* (1953). In an ingenious series of experiments these workers found evidence of the presence of an intracranial volume centre, sensitive to hydrostatic pressure and regulating the excretion of salt. Unfortunately this volume centre was not found to be active in patients with congestive failure; neck compression failed to cause a significant increase in sodium excretion with the patient sitting, and the influence of posture was very slight.

Granted that the sequence of events, inadequate cardiac output leading to renal shut-down, is the main determinant of salt and water retention in heart failure, it may be that reduction of blood flow to other tissues contributes to the overall state of congestion. Relatively anoxic muscles may produce the vasodepressor material of Shorr (1951), and this has been shown to have an antidiuretic effect mediated through the pituitary. Impaired hepatic blood flow may not only lead to further liberation of vasodepressor material, but may also slow its vasodepressor material inactivation system. Similarly, the liver may fail to inactivate as efficiently as in normals the antidiuretic hormone of the pituitary and the suprarenal corticoids.

Studies of the electrolytes in patients with heart failure have been contributed by Iseri *et alii* (1955). Muscle analyses showed a potassium concentration 30% less during failure compared with the concentration present on recovery. Acute and chronic physical stress caused a rise in plasma sodium concentration when patients were given an oral salt load. The rise in serum sodium content occurred in normals; but the rise in patients with heart failure was much greater, and with the same amount of exercise was approximately proportional to the severity of the heart failure. The authors interpreted their findings as follows:

1. Physical activity in the presence of an inadequate circulation causes a rise in intracellular osmotic pressure of muscle due to activation of osmotically bound base. Sodium and potassium pass from the cells into the extracellular fluid and/or extracellular water passes into the cells.

2. The kidney retains sodium perhaps under the influence of aldosterone; water is retained due to secretion of antidiuretic hormone with rise in the osmotic pressure of extracellular fluid.

3. If the patient has sufficient rest the reverse process will occur; in severe heart failure sufficient rest may be impossible, and with renal shut-down there will be permanent retention of salt and water.

Lowe has contributed interesting studies of the cyclic changes in fluid loss and retention in patients with œdema from heart failure. His work suggests that one factor in the control of body water is a mechanism sensitive to volume changes. The two types of patients with cardiac œdema (Lowe, 1950) would, on the basis of the previous discussion, correspond to two stages in the progress of cardiac insufficiency.

Figure I is a summary in diagrammatic form of the preceding discussion.

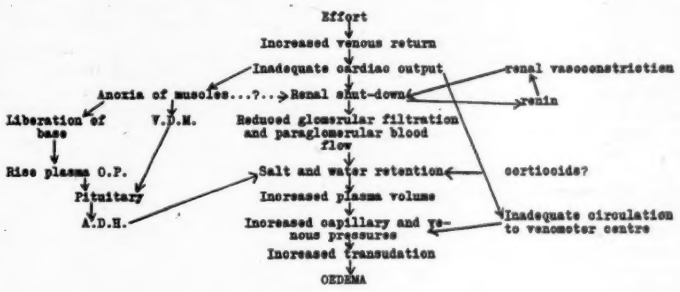

FIGURE I.

In the foregoing schema the main unknowns are the factor causing and controlling renal shut-down and the degree to which the suprarenal corticoids are involved. It is known that renal shut-down is not under sympathetic control, because it occurs after sympathectomy has been performed. The control of renal hæmodynamics seems to be the most promising field for further investigation.

According to some workers, salt and water retention is beneficial to the hæmodynamics of heart failure—the best result that can be obtained under difficult circumstances. This view is held by those who consider that the heart is sensitive to atrial filling pressure (Starling and Borst), but according to Warren and Stead there is no close relation between cardiac output and atrial filling pressure, and certainly the patient with heart failure is improved by loss of œdema and reduction of venous pressure to normal. It seems more likely, then, that salt and water retention is the unavoidable consequence of renal shut-down. That this latter mechanism is useful in so far as it diverts blood to other relatively ischæmic tissues, but that it is a mechanism more suited to shock—an emergency of short duration—than to chronic irreversible heart failure, in which continued fluid retention makes the subject much worse and requires active treatment for prevention and relief.

Conclusions.

In the train of events leading to fluid retention it seems to the present writer that a relative anoxia of muscle is an essential feature. That tissue anoxia is a factor is suggested by the occurrence of congestive failure in association with a high cardiac output in anoxic pulmonary disease, severe anæmia and beriberi. In the first two conditions there is a diminished blood oxygen content, whilst in the last-mentioned the transfer of oxygen to the cells is impaired through a defect in the cytochrome system. It is clear that when there is diminished blood oxygen content adequate tissue oxygenation can be maintained only by an increased blood flow and a rise in the oxygen utilization index. One may similarly expect failure with a high output when blood is shunted from the tissues, as in Paget's disease or an arteriovenous aneurysm, or when tissue metabolism is increased from thyrotoxicosis. Thus if tissue anoxia is a factor, one would expect high output failure in just those conditions in which it is found to occur.

The following hypothesis then seems likely. The common factor in low and high output failure is inability of the circulation to supply adequate oxygen to the tissues, in consequence of which certain changes occur leading to fluid retention. The presence of central cyanosis is not a

reliable indication of tissue anoxia because of the compensating mechanisms mentioned above, and in addition there is often polycythæmia, which increases the likelihood of pronounced cyanosis at the same time as it increases the capacity of the blood for oxygen. Since the oxygen tension of the blood is normal in the common forms of heart failure, a diminished oxygen tension cannot be an important or necessary factor in the production of œdema.

When heart failure is of gradual onset it will first be evident only on exertion. Thus fluid retention occurs with activity during the day and the excess is excreted at night, when the heart can supply adequate blood for the smaller tissue needs. With exertion the increase in cardiac output may normally rise many litres, to be four or five times the output at rest.

By far the greatest part of this increased output is expended in increased blood flow through muscles, and in fact the increased flow through muscle is made even greater by shunting of blood from other tissues. The neuro-hormonal factors controlling vasoconstriction in these tissues (splanchnic area and skin) do not, it seems, control the renal blood flow. However, from a phylogenetic point of view, because of the large amount of blood involved in the renal blood flow one would expect renal shut-down with severe exertion to be a mechanism giving a great evolutionary advantage to those who possessed it. Further suggestive evidence is provided by the occurrence of renal shut-down in shock. This latter syndrome resembles heart failure in its essential feature—inadequate cardiac output—so it is to be expected that the consequences will be similar in both. Again, because of the large changes that occur in heart output it is difficult to see how the suprarenal glands or the pituitary could be primarily affected.

For these reasons it seems most likely that if tissue anoxia is involved in heart failure then it is muscle rather than any other tissue that is anoxic. This leads to the further speculation that anoxic muscle produces some substance which causes renal shut-down and perhaps an increased secretion of suprarenal corticoids. The discovery of such a substance added to the electrolyte changes already demonstrated by Iseri *et alii* would give adequate explanation for fluid retention in heart failure under all the circumtances in which it is found to occur. Moreover, this train of events gives a rational explanation for the common clinical observation that rest is of the utmost benefit in all types of heart failure, and that in the early stages rest alone is sufficient to restore the disordered circulation to normal.

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CEREBELLAR ABSCESS.

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WITHOUT doubt, cerebellar abscess is the meanest, the most silent and the most unpredictable neurosurgical condition I have ever encountered. Usually it presents the classical symptoms and signs of compression, as in the case of any other cerebellar expanding lesion. On occasions, however, it may be as silent as the grave and may produce no localizing signs whatsoever. In its more mischievous moods it may even produce totally remote signs, which merely serve to present a false trail, as does the curlew in order to lead us far away from her nest. To my everlasting regret, I have experienced such humiliating circumstances in which the silent type of cerebellar abscess has been present, and, to use a colloquialism, I have sadly missed the boat.

In my own meagre experience with cerebellar abscess I have been able to recognize and treat the condition successfully in most cases. In these there were sufficient cerebellar symptoms and signs, following an ear infection, to localize the lesion accurately. In two cases, however, there were no localizing cerebellar signs present at all, and in one of these there were even false localizing signs pointing to the cerebrum as the seat of the lesion. As a result of my experience with these two cases I decided to explore the posterior fossa in all cases in which a temporal lobe abscess was suspected, but not found at operation. In one subsequent case this resolution paid dividends, although the lesion turned out to be a cystic collection of fluid rather than an abscess.

This latter case was that of an elderly woman who had a history of a discharging ear over a long period, and who developed severe headache and later became very drowsy. The obvious thing to suspect was a temporal lobe abscess, but at operation none was found. Acting on my resolution I then explored the corresponding cerebellar hemisphere and there found a large cystic collection of clear fluid. This was aspirated, and the patient made an uninterrupted recovery. From a mechanical point of view the fact that the lesion was a cyst and not an abscess is inconsequential. I feel that this was purely circumstantial and that the principle remains the same.

In dealing with neurology and neurosurgery, that rather mysterious branch of medicine, one must realize that the

central nervous system can be a very temperamental and unpredictable lady. It does not always act as a man-made mechanical brain which produces the required result at the appropriate moment. Numerous totally different diseases are capable of producing the same identical syndrome. On the other hand, a single disease is capable of producing a great variety of syndromes. Syphilis and tuberculosis, for example, are well known for the large variety of symptoms and signs that they may cause. It is for this reason that it is so difficult to classify the chronic demyelinating and degenerative diseases from the viewpoint either of their symptomatology or of their underlying pathological processes. It is undoubtedly true that the more we become acquainted with disease of the central nervous system the less dogmatic and the more humble we become. Personal experience is by far the greatest teacher, and as the years roll by we pick up little tit-bits that may seem inconsequential at the moment but which may prove invaluable on some future occasion.

Fortunately, cerebellar abscess is a rare condition, and for my part I think I have seen less than a dozen cases in my twenty-odd years of neurosurgical experience. This provocative condition usually results from the direct spread of infection from a middle ear or mastoid infection. In the vast majority of cases this infection spreads into the temporal lobe or into the temporo-occipital region, but occasionally it spreads downwards into the posterior fossa. Following a discharging ear, the occurrence of even such vague symptoms as headache, drowsiness or blurring of vision must make one suspect the presence of an abscess. In such cases the temporal region must be explored as the most likely site. If no abscess is found in that area the corresponding cerebellar hemisphere should then be suspected and also explored. Much as I dislike exploratory operations on any part of the brain, I feel that under such circumstances there is nothing else left to do.

Cerebellar abscess acts in the same way as any other expanding lesion, and produces most of its symptoms and signs by pressure on the neighbouring structures. These may result from interference with the function of the cerebellum or with certain centres in the pons and medulla, or from obstruction to the cerebro-spinal fluid pathways. Interference with cerebellar function may produce ataxia, incoordination and hypotonia. Pressure on the pons may cause nystagmus, weakness of the sixth and seventh cranial nerves, or even involvement of the pyramidal tracts. Obstruction of the cerebro-spinal fluid pathways may cause an increase in the intracranial pressure, with possible headache, blurring of vision, papillœdema and vomiting. If any localizing cerebellar signs are present, the solution is usually simple; but when there are only one or two generalized symptoms due to increased pressure it may not be possible to localize the lesion with any degree of accuracy. Under such circumstances the temporal region should be the first suspect and should be explored. If the result of this is negative, then the corresponding cerebellar hemisphere should be the next suspect and (I speak purely from my own experience) should also be explored.

In view of the rarity of cerebellar abscess it is not surprising that there has been so little published in the literature on the subject. Ramadier *et alii* in 1935 furnished a very comprehensive report and in their total number of autopsies they found that cerebellar abscess occurred in only 0·08% of cases, practically all of which arose from some ear infection. They stated that it was not possible to localize the abscess to the cerebellum; nor was it possible to estimate its size because of the added influence of the accompanying cerebellar œdema. They also stated that sudden death from bulbar respiratory syncope was almost always due to the presence of an unsuspected second abscess cavity. Cerebellar abscess may heal spontaneously and produce no further symptoms. Shapiro, in 1937, reported a case in which there were symptoms and signs suggestive of a cerebellar abscess, but these subsided without operation. Some time later the patient died from another cause and at autopsy there was found an old well-healed abscess in the cerebellum.

The following reports of cases are presented to illustrate the points that have been mentioned above. In one way the result in the first case was highly satisfactory in that the cerebellar abscess was localized accurately and operated upon successfully, the patient making, temporarily, a perfect recovery. Unfortunately, as so often happens in surgery, the operation was successful but the patient died.

The patient was an elderly man who gave a history of bilateral discharging ears for many years. One month prior to his admission to hospital he developed vertigo, especially when lying on his left side. Later he started vomiting and complained of severe pain in the back of his neck. On admission to hospital he was drowsy and slow in his mental reactions. His powers of concentration were poor, but he was cooperative up to a point. There was fairly severe neck rigidity, and nystagmus was noted later. The cerebro-spinal fluid pressure was 150 millimetres, the cell count was 15 per cubic millimetre (mainly lymphocytes), and the protein content was 110 milligrammes per 100 millilitres with an increase in globulin content.

When I was first requested to see him I felt that the evidence was sufficient to indicate an intracranial abscess, and I advised an exploration of the temporal lobe. Later, when he was transferred to our neurosurgical unit, I reconsidered and decided to attack the cerebellar hemisphere first. I located the abscess and aspirated about seven cubic centimetres of purulent material and injected penicillin and streptomycin into the cavity. During the following two days he made a remarkable recovery, in that he became fully conscious and his neck stiffness disappeared, although the nystagmus remained. On the third day after operation his condition deteriorated and he lapsed into a semiconscious state again, responding only to painful stimuli. The abscess cavity was again aspirated and a further four or five cubic centimetres of pus were removed and antibiotics injected. Again he made a complete recovery. At the end of a week he was symptom-free and it was decided to allow him up on the following day. The sister in charge happened to be doing her rounds later in the day and noted that the patient was perfectly well. She spoke to the man in the next bed and within a matter of seconds glanced back to the patient. She saw that he was unconscious and not breathing and was deeply cyanosed, and when she examined him it was obvious that he was dead. One curious thing that she reported was that at that moment she noticed a "horrible smell".

Permission for autopsy unfortunately could not be obtained, so that the reason for his sudden death is still a matter of conjecture. The "horrible smell" experienced by the sister in charge might suggest the rupture of a lung abscess. The statement of Ramadier *et alii* must also be considered, in which they reported that sudden death in such circumstances was due to a second unsuspected cerebellar abscess. In such circumstances, however, it would be difficult to imagine the presence of a "horrible smell", but there are many other possible causes of such a sudden death. This case is presented only to show that although the diagnosis and operative treatment were correct there was something that was missed.

The following two cases proved to be of the silent type and these were the two in which I really "missed the bus".

The first patient was a middle-aged man whom I saw some seven or eight years ago. He had complained of a discharging right ear for about ten years and over the previous six weeks had complained of headache, starting in the occipital region and later spreading to the frontal region. The headache was originally intermittent but gradually became constant and prevented sleep. During the few days prior to admission to hospital he complained of a stiff neck. He was admitted to the Royal Prince Alfred Hospital, and the only abnormalities found on examination were deafness in the right ear and neck rigidity. The cerebro-spinal fluid pressure was 150 millimetres of fluid, and the fluid was turbid with 2800 cells per cubic millimetre, 75% being polymorphonuclear cells. A right radical mastoid operation was performed, and the brain was needled in five directions, but no cerebral abscess was found. He still remained ill, but further lumbar punctures all revealed the pressure to be within normal limits. The cell count gradually subsided and changed to 95% lymphocytes, and all attempts at culture failed to produce any organisms. The whole picture was that of an acute meningeal infection gradually subsiding.

I was first asked to see this man two days after his admission to hospital. I felt, from his story and examination,

that there was no evidence of an abscess, but that his condition was purely due to meningitis. I was again asked to see him some eighteen days later as his condition was still not satisfactory. I could still find no evidence of a localized abscess, but in view of the time element I advised ventricular air studies to be on the safe side. A ventriculogram was prepared some ten days later, even though his condition had greatly improved, and this showed a very slight generalized dilatation of the ventricular system with the ventricles in their normal position. I felt that this slight dilatation could well have been due to the meningitis. However, in attempting to visualize the aqueduct and fourth ventricle, by use of the vertex-down position, it was noted that the air was not seen below the upper end of the aqueduct. This made one think of a posterior fossa lesion, but in view of the normal cerebro-spinal fluid pressure, the diminished cell count, the absence of cerebellar symptoms and signs, and the relatively normal ventriculogram, I decided not to do anything surgically at the moment but to keep a close watch on the patient. He continued to improve for several days, but then he suddenly collapsed and died within a few minutes. Permission for autopsy was obtained, and this revealed quite a large abscess in the right cerebellar hemisphere.

The second example was presented to me a few months ago; unfortunately, at that time the first case had faded from my memory.

This was the tragic story of a young woman who also had the silent type of cerebellar abscess. In this case not only did the abscess fail to produce any localizing cerebellar signs, but there were actually signs which could have pointed only to the face area in the right motor cortex of the cerebrum. Some seven days before I was first requested to see her she was discharged from hospital after a right radical mastoid operation, and her condition was reported to be very satisfactory. On the day after she returned to her home she began to vomit and became progressively drowsy. The vomiting eventually ceased, but the drowsiness continued, and later she became irritable and developed photophobia. Five days after she had returned home she was taken to the out-patient department for a check-up. On her way home she began to vomit again and lapsed into a semiconscious state. Headache then came on and eventually she was literally screaming with pain.

She was readmitted to hospital as an emergency measure and shortly afterwards she had a focal Jacksonian epileptic seizure. This attack started with twitching of the left side of her face and gradually spread until it became generalized. Such an epileptic seizure could have originated only in the face area of the right motor cortex, just above the temporal lobe. As events turned out, this focal seizure proved to be merely a false trail. Its underlying cause is problematical, but it could not have originated in the cerebellum. It is possible that there was some inflammatory reaction in the neighbouring temporal lobe, without actual abscess formation, with resulting cerebral œdema, in which circumstances an epileptic seizure could well occur.

I was asked to see her shortly after her readmission to hospital, and I found her to be responsive but quite uncooperative. Apart from some slight blurring of her optic discs there were no abnormal neurological signs. The electroencephalogram revealed a marked generalized slow wave dysrhythmia, in which one to three cycles per second waves were prominent, but there was no evidence of any local abnormality. This recording merely indicated that there was a generalized disturbance of cerebral function which because of the history could have been caused by multiple cerebral abscesses. My impression was that she had a right temporal lobe abscess, and I advised operation.

She was transferred to the neurosurgical unit and I explored her right temporal lobe, but did not find any abscess. The brain needle entered the temporal horn of the lateral ventricle, which appeared to be in its normal position, and the fluid pressure was low. A few cubic centimetres of air were injected and X-ray pictures were then taken. The films showed the ventricles to be absolutely normal in size, shape and position, which completely excluded a supratentorial expanding lesion. The girl was then sat upright and about 20 cubic centimetres of air were injected via the lumbar route. These films showed the air passing upwards freely through the fourth ventricle and aqueduct into the third anl lateral ventricles, and there was no distortion to suggest a posterior fossa lesion.

At this point we were at a standstill, with no light to guide us. A diagnosis of cerebellar abscess was considered, but this was disregarded because of the negative evidence already described. I finally decided that her symptoms were due to cerebral œdema of toxic origin, resulting from the adjacent infection in the petrous portion of the temporal bone. On the basis of this assumption she was given magnesium sulphate enemata twice daily, but she showed little improvement. I then performed a bilateral subtemporal decompression and after this she became fully conscious before she was removed from the operating table. So we breathed freely again and felt that the problem had been solved. About half an hour after she had been returned to her ward the nurse in attendance noted that she suddenly stopped breathing. Artificial respiration, intubation, and administration of oxygen and various drugs proved of no avail and she died. The unkindest cut of all was that the autopsy revealed a large abscess in the right cerebellar hemisphere.

My first thought was that the Australian expression "You can't win" would fit the situation perfectly. If I had remembered the case that I had met with several years previously I feel that this girl's life would probably have been saved; but at the critical moment it did not come to my mind.

In summarizing this paper I can do little more than repeat that cerebellar abscess usually presents sufficient symptoms and signs to enable the neurosurgeon to localize the lesion accurately. Occasionally, however, it may present but few general symptoms, such as headache or dimness of vision, without any localizing signs whatsoever. Even such vague symptoms occurring in a person with a history of a discharging ear should make one think of a temporal lobe abscess. If an abscess is not found in this area, then one should consider the possibility of the infection having spread downwards into the posterior fossa. In such circumstances I feel that the corresponding cerebellar hemisphere should be explored. The operation is not a major one and if no abscess is found no harm is done, but if an abscess is found it may well save a life.

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Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand: Gordon and Gotch (Australia), Limited. Subscription for twelve months: 20s. (sterling), including postage.

THE regular features of *Family Doctor* are a most important part of its make-up, particularly the home items which are now incorporated into a home service supplement, the "under five" forum which explains itself, the answers to correspondence and the readers' letters to the editor. In addition to these, the May, 1956, issue contains articles on children with asthma, vitamins, schools of an unusual kind and the photographing of patients in hospitals, organized play for children, baby teeth, the education of the subnormal and a variety of other things. A special attractively produced supplement provides a meal plan for the summer. The May issue is as attractive as ever and can be heartily recommended.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Operative Technique in Specialty Surgery", edited by Warren H. Cole, M.D., F.A.C.S., with an introduction by Allen O. Whipple; Second Edition; 1956. New York: Appleton-Century-Crofts, Incorporated. 9½" × 6½", pp. 989, with many illustrations. Price: $20.00.

This volume is divided into 21 sections, the subjects ranging from surgery of the heart and great vessels through the different systems to gynæcological surgery and surgery of the male genito-urinary system. There are 32 authors.

The Medical Journal of Australia

SATURDAY, JUNE 30, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

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A REPORT ON THE NATIONAL HEALTH SERVICE OF GREAT BRITAIN.

In May, 1953, the Minister of Health of Great Britain and the Secretary of State for Scotland appointed a special committee with the following terms of reference:

> To review the present and prospective cost of the National Health Service; to suggest means, whether by the modifications in organization or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made available; to advise how, in view of the burdens on the Exchequer, a rising charge upon it can be avoided while providing for the maintenance of an adequate Service; and to make recommendations.

The membership of the committee was as follows: C. W. Guillebaud, C.B.E., Dr. J. W. Cook, F.R.S., Miss B. A. Godwin, O.B.E., Sir John Maude, K.C.B., Sir Geoffrey Vickers, V.C. The report of this committee was presented to Parliament by command of Her Majesty in January, 1956, and has been published.[1]

It will, of course, be impossible to give any account of the whole of this voluminous report; it covers all aspects of the subject. We shall have to be content with some of the aspects which seem most likely to interest Australian practitioners. The scope of the document will best be shown by a short statement of the way in which it is divided into eight parts. Part I deals with the present and prospective cost of the national health service in England and Wales. The changes in resources used by the National Health Service are summarized and the future trends in the cost of the service are discussed. Part II deals with the general structure of the National Health Service and Part III with the hospital and specialist services. The family practitioner services are discussed in Part IV, and here special sections are devoted to general dental services and supplementary ophthalmic services. In Part V local health authority services are dealt with and in Part VI the Whitley Council machinery. Part VII is headed "General", and Part VIII consists of a summary of conclusions and recommendations. There is an extra section containing "reservations"; it is by Sir John Maude and is a kind of minority report.

The current net cost of the National Health Service in England and Wales in productive resources in the year 1953-1954 reached £430,500,000, having increased roughly by £15,000,000 each year since 1949-1950. Between 1948 and 1954 there was a rise in population of nearly 2%. When allowance is made for this and for changes in the age structure of the population, the cost per head at constant prices was almost exactly the same in 1953-1954 as in 1949-1950. However, trends of expenditure have been different in different parts of the service. Between 1949-1950 and 1953-1954 net current expenditure on the hospital services rose by £71,000,000 and that on local authority services by £11,000,000, while expenditure on Executive Council services fell by £24,000,000. Naturally these divergent trends have to be taken into account when one is considering possible future trends. No attempt, we read, can be made to forecast how the cost of the National Health Service is likely to vary in, say, the next twenty years. Some conclusions are quoted from a work on the effect of demographic and other social factors on the demand for hospital care and the effect of projected population changes on the future cost of the service. Two of these may be mentioned. In the first place, an analysis of the Government Actuary's estimates of the population of Great Britain in 1979 shows that among those who make much the heaviest claims on hospital accommodation, the number of women of pensionable ages will actually decline, while the number of single men of such ages will increase by only a negligible figure. In the second place population changes by themselves are not likely to exert a very appreciable effect on the cost of the National Health Service.

There is a fairly long discussion on what constitutes an "adequate service"; this is one of the most important aspects of the report. Incidentally it is referred to in the "final comment" of the whole document. "If the test of 'adequacy' were that the Service should be able to meet every demand which is justifiable on medical grounds, then the Service is clearly inadequate now, and very considerable additional expenditure (both capital and current) would be required to make it so." It is necessary only to mention the deficiencies which would have to be made good in the provision of mental hospitals, mental deficiency institutions, services for the chronically sick, hospital outpatient departments, domiciliary health services and so on, in this regard. Any attempt to produce adequacy would mean that a greatly increased share of the nation's human and material resources would have to be diverted from other uses. Moreover, it is not clear that if the service became "adequate", it would remain so without

[1] "Report of the Committee of Enquiry into the Cost of the National Health Service"; 1956. London: Her Majesty's Stationery Office. 9¼" × 6", pp. 321. Price: 9s. net.

continually increasing expenditure. It would, of course, be possible to enlarge on this aspect of the discussion almost to further orders. There is one entry on the other side of the ledger to be borne in mind, and that is that the National Health Service is wealth-producing as well as health-producing. Improved health means improved efficiency in industry; money spent on the National Health Service "may properly be regarded as 'productive'—even in the narrowly economic sense of the term". The conclusion, as may be expected, is that in the absence of an objective and attainable standard of adequacy, the aim must be to provide the best service possible within the limits of available resources. We read that it is still sometimes assumed that the Health Service can and should be self-limiting, in the sense that its own contribution to national health will limit the demands made upon it to a volume which can be fully met. "This, for at least the present, is an illusion."

Reference must next be made to the general practitioner and the hospital service. The committee welcomes the recommendations made in the Scottish Report and the Cohen Committee's Report for improving the integration of the general practitioner and hospital services. It mentions recommendations which it regards as of great importance. These have to do with the provision of hospital beds for the use of general practitioners; the provision of clinical assistantships for general practitioners; the availability to general practitioners of diagnostic facilities in hospitals, particularly for X-ray and pathological examinations; the development of a close liaison between hospital doctors and general practitioners; the recognition, in the organization of hospital and specialist services, of the needs of the general practitioner; the recognition that the role of the hospital out-patient department should be in the main consultative; the acknowledgement of the general hospital as a centre of medical endeavour where the general practitioners in the area have right of entry and can meet their hospital colleagues on terms of equality. In order that the National Health Service shall operate in the most efficient and economical way, it is thought desirable that whenever practicable patients should be treated in their own homes by the general practitioner and the local health services, instead of being admitted to hospital where the running costs are high. When a patient is admitted to hospital "he should be discharged at the earliest possible date, any necessary follow-up treatment being provided either in the hospital out-patient department or at home by the general practitioner and the home health services". Patients are not kept in hospital nowadays any longer than is necessary. Already in some parts of Australia there is being developed a kind of day nursing service acting in conjunction with hospitals, and in this way many "hospital-patient-days" are saved. The committee, in discussing local health authority services in the summary, states that the provision of domiciliary health services is essentially a "local authority function". Whether this statement can be accepted depends on what is meant by domiciliary health services. It clearly does not include ordinary medical attendance in the home and should not include follow-up treatment after discharge from hospital. The powers of local health authorities are set out as having to provide the following services: health centres, care of mothers and young children, domiciliary midwifery, health visitors, home nursing, vaccination and immunization, ambulance services, prevention of illness and after care, domestic help, mental health. The functions of a local health authority may be exercised only after the Minister of Health has given his approval to detailed proposals for providing the service concerned. It may not be quite fair to state these functions in that blunt and abbreviated way, but Australian practitioners will have no difficulty in recognizing which or what part of the powers ceded to local health authorities under the British Act would in their opinion be most suitably carried out by the private practitioner, if necessary in collaboration with the local authority. As a matter of fact the committee notes, as one of the improvements to be effected, the development of home health services and their closer integration with the general practitioner, hospital and welfare services. However, as far as the National Health Service vote is concerned, it knows of no wide fields in which large sums of money might be expended at the present moment in order to bring the preventive health services more into line with the curative services.

In the matter of prescriptions two statements are to be noted. The first is that the committee is not in favour of the introduction at the present time of a limited list of prescribable drugs in the National Health Service. A useful suggestion in this respect is that every effort should continue to be made to keep doctors informed about the cost of general prescribing in order to "stimulate them to review carefully their prescribing of expensive drugs and the quantities prescribed". The other statement is that the committee has no reason to think that the shilling prescription charge hinders the proper use of the service by at least the great majority of potential users. It does not think that the removal of the charge at the present time would improve the working of the service to an extent commensurate with the cost.

The committee finds that the maternity services are "in a state of some confusion, which must impair their usefulness, and which should not be allowed to continue". "We are told that the present structure appears to represent a not very satisfactory compromise between the services which were in existence before the Appointed Day and the new maternity medical service which was introduced with the National Health Service." In other words the service has slipped since it was introduced. The time has come "for an appropriate body to review the whole of this field to find out precisely what services . . . are needed. . . ." The respective roles of local authority, general practitioner and hospital out-patient department have to be determined. In Britain ideas on this matter differ from those held in this country, where the general practitioner is by common consent assigned the leading role in maternity and child welfare services.

The commiteee's "final comment" has been mentioned—that in practice there is no objective and attainable standard of adequacy and that no major change is needed in the administrative structure of the National Health Service. In addition no opportunity has been found for making recommendations which would either produce new sources of income or reduce in a substantial degree the annual cost of the service. Further, it is impossible to forecast whether the cost of the service in the more distant

future will increase or become less. Admittedly there are defects in the present organization and administration of the National Health Service, but the committee has reached the conclusion that so far the record of performance has been one of real achievement. Perhaps it was this sentence which induced *The Times* to start its leading article on the report with the remark that it would be quite unfair to dismiss the Guillebaud Report as a blue book full of whitewash. That, of course, is true—the defects have been shown up and we have referred to some of them. One important remark by the committee should be recorded—that not a few of the long-term problems of the National Health Service will be solved only by the medical profession itself. We can apply this remark to our own medical services in Australia.

Current Comment.

GLAUCARUBIN IN AMŒBIC DYSENTERY.

THE treatment of amœbiasis is difficult and in the chronic state frequently unsuccessful. The problem of therapy is not primarily one of resistant organisms, but one of effectively reaching the organisms with a sufficient quantity of a lethal concentration of the prescribed drug. The amœbæ may be in the intestinal contents or on the surface of mucosa, or they may be buried deeply in the tissues. In chronic infections there may be extensive and mixed bacterial infections with fibrosis and permanent local damage of the affected intestinal tract. Further complications are the development of amœbic hepatitis and the formation of amœbic abscesses. Final preventive measures lie in the sterilization of the carriers who pass on the cysts and who may or may not be symptomatic themselves. The ideal amœbicide must play the dual role of reaching a high concentration in the intestinal tract and of being absorbed in concentrations sufficiently high in the deep tissues. In the long-standing case after repeated treatments the *Entamœba histolytica* develops resistance to combinations of drugs and the outlook for ultimate cure is poor. There are five groups of drugs effective to some extent in the treatment of amœbiasis. These are the arsenical compounds such as carbasone, the halogenated hydroxyquinolines such as "Diodoquin", 4-aminoquinoline such as chloroquin diphosphate, the ipecacuanha derivatives such as emetine hydrochloride, and the new antibiotics such as "Terramycin".

These treatments are all highly effective in the acute amœbic infections, but many chronic cases have proved resistant to the most vigorous therapy including that of the antibiotics. Compounds possessing potent properties as amœbicides have been isolated recently from several plants of the simarouba genus, particularly *S. amara* and *S. glauca*. The effectiveness of these extracts has been known for some considerable time and various local preparations enjoy popular use in Mexico. However, only recently has a pure product of constant activity been developed. Various experimental studies have shown the new product glaucarubin to be effective and safe in the elimination of amœbiasis in dogs, rats and guinea-pigs. E. C. del Pozo and M. Alcaraz[1] have used glaucarubin in the treatment of human amœbiasis. The drug was administered to 87 infected patients whose infections were proved by laboratory diagnosis, 78 of the infections being chronic in type. The drug was finally administered by mouth in a dosage of three milligrammes per kilogram of body weight per day for five days. The daily dosage was divided into three parts. This schedule and these amounts were reached after the careful use of increasing amounts in different groups of the patients. At the start of treatment each patient had large quantities of the cystic forms of *E. histolytica* in the fæces. Each of the 78 patients with chronic infections had, in variable degree, signs and symptoms of chronic amœbiasis. In every patient clinical improvement occurred at the third or fourth day of treatment, including those patients in whose fæces the parasite was still found. In no case were significant toxic reactions observed, and the signs of chronic amœbiasis completely disappeared when these were due to the *E. histolytica*. Each of the acute amœbiasis patients had great numbers of mobile *E. histolytica* trophozoites in the fæces. The clinical response was spectacular. After twenty-four hours of treatment the diarrhœa diminished and between the second and fourth days mucus and blood disappeared from the fæces, which became of normal type. Of the nine acutely ill patients, seven were cured at the first course of treatment and the other two required a repeated course. No eventual relapses were recorded and in each case the tolerance to the glaucarubin was satisfactory. Of the 78 patients with chronic amœbiasis, many were treated with small doses of the drug before the standard schedule was conceived. Even with relatively small doses the *E. histolytica* disappeared from the stools in all but four of 40 patients, and in seven others of this group relapse eventually occurred. Of the 38 patients who received the full course of the drug, none developed toxicity, in each the organism had disappeared from the fæces by the fourth day, and only one patient had a relapse three months later. Blood counts, white cell differential counts, and liver and kidney function tests performed on samples of the patients failed to reveal any changes due to the treatment.

It thus appears that glaucarubin may well be a powerful and safe therapeutic agent in the treatment of acute and chronic amœbiasis. Relapse did occur in eight of the patients with chronic amœbic dysentery, but only one of these had received the full dosage of glaucarubin suggested by Pozo and Alcaraz on their experiences in this trial.

[1] *Am. J. M.*, March, 1956.

SULPHONAMIDES AND DIABETES.

THE article by Dr. Ewen Downie and his three colleagues from the Alfred Hospital, Melbourne, published in this issue, is of more than passing interest. It brings to the direct notice of Australian medical practitioners a subject which has been engaging the attention of clinicians and laboratory workers on the other side of the world for the last few months. Those who read their medical journals regularly will recall that a leading article entitled "Sulphonamide Compounds for Diabetes" was published in the *British Medical Journal* of December 10, 1955. This article made it clear that, though it was reported by Janbon *et alii* in 1941 that a sulphonamide derivative lowered the blood sugar level in man, observations which were confirmed by other workers, it remained for German workers in 1954 and 1955 to carry the work further and apply it to human patients. When Dr. Downie was in America recently he attended discussions on this subject. This conference is mentioned in a leading article in *The Journal of the American Medical Association* of April 14, 1956. In this article it is stated that information is available on only two of the sulphonamide preparations that have been investigated in this connexion—1-butyl-3-sulphanilyl-urea or "Carbutamide", and 1-butyl-3-9-tolyl-sulpho-nylurea or "Tolbutamide". Only the former of these two compounds was dealt with at the conference. Dr. Downie also mentions 1-butyl-3-*p*-toluene-sulphonylurea or "Orinase". In the treatment of his 14 patients he used "Carbutamide"; his case histories should be studied with care. It will be noted that Downie *et alii* and the editorial in the *British Medical Journal* refer to work by German observers; the references are all to German journals. Articles from the three groups of German authors are now available in English in the first issue of the *German Medical Journal* (the whole journal is in the English language) issued from Stuttgart in January, 1956. H.

Franke and J. Fuchs write on "A New Anti-Diabetic Principle", J. D. Achelis and K. Hardebeck on "A New Blood Sugar Reducing Substance", and F. Bertram, E. Bendfeld and H. Otto on "An Effective Oral Antidiabetic Drug (BZ55)". Attention must also be drawn to an article by A. S. Ridolfo and W. R. Kirtley appearing in *The Journal of the American Medical Association* and relating some clinical experiences with "Carbutamide". The patients treated by these authors numbered in all 31, but seven of them were treated as out-patients only and 11 were treated in hospital. It is from the last-mentioned group that most of the conclusions are drawn. The aim of treatment was to maintain the "Carbutamide" at a minimum level of 10 milligrammes per 100 cubic centimetres of blood. In the mature, obese, relatively mild diabetics the results were gratifying, so that in five such patients insulin was no longer needed; in the others the drug was a complete or partial failure. Selection of likely out-patients of the overweight, mildly diabetic type confirmed the success of "Carbutamide" in this type of patient. Franke and Fuchs found in the first instance that BZ55 (as the drug is known in Germany) when administered by mouth to healthy persons produces a considerable lowering of the blood glucose levels and symptoms of hypoglycæmia. They found that the compound was rapidly absorbed and was in detectable amounts in the blood within thirty minutes. Hypoglycæmia occurred within two to three hours and the blood sugar returned to normal in about six hours, though the sulphonamide remained in detectable quantities in the blood-stream after twenty-four hours. In untreated diabetic patients the administration by mouth of BZ55 resulted in the reduction or disappearance of glycosuria. In treated diabetics the dosage of insulin could be reduced or even omitted when BZ55 was taken. As with insulin, the dosage of BZ55 varied with individuals, but in a series of fifty patients Franke and Fuchs found that the average maintenance dosage, after a loading schedule, was from 1·0 to 1·5 grammes daily. In their series the desired effects were obtained in 80% of the patients. No toxic side effects have been noted in a year of such treatment.

In what they call their preliminary report Achelis and Hardebeck state that BZ55 fulfils all the requirements of a good sulphonamide in its bacteriostatic activity. In experimental animals, the hypoglycæmic effect was profound and was the only contraindication for its use in infections. The hypoglycæmic effect persisted for at least twelve hours, though in passing it is to be noted that the dosage was much higher than that used in the human trials of Franke and Fuchs. The acute toxicity level in mice was 11·5 grammes per kilogram of body weight and with a lower dosage there appeared to be some accumulative action.

Bertram, Bendfeldt and Otto have used BZ55 in the treatment of 82 patients suffering from *diabetes mellitus* of varying severity and duration. The maintenance dosage was in the region of 1·0 gramme daily in two doses. The results among the older diabetics were particularly good, although by no means uniform. In only three of 28 older diabetics was BZ55 ineffective and insulin necessary. In several patients glycosuria disappeared and blood sugar levels approached normal. Some patients did not even relapse when the treatment was withdrawn, provided that the strict diet regime was maintained. In 28 out of 38 older diabetics BZ55 completely replaced the previous insulin. In this group of patients there was also a variable tendency for the metabolic improvement to continue when BZ55 was withdrawn. The results in the treatment of young diabetics were disappointing; in no case could insulin be withdrawn, though in some patients the dosage could be reduced. No significant side effects were found and there was no adverse effect on diabetic metabolism. There was no sign of decreasing response with continued use of the drug, and in no diabetic patient was hypoglycæmic shock produced despite the occasional use of high dosages of BZ55.

It will be seen that the findings of the observers named differ very little. The new substance does not act in the way that insulin acts; we cannot say that its use is a substitute for insulin therapy. As Dr. Downie makes quite clear, the mode of action is not known. The German authors have postulated a selective action on the α cells of the pancreas and it is possible to build up a workable theory on this basis. Only the future will reveal the true state of affairs. In the meantime this form of treatment should be used only under controlled observation. The dissemination of information on these drugs among the public, by broadcasting and other methods, is greatly to be deplored.

ALDOSTERONE.

As a result of researches carried out over many years and in several places a number of steroids have been isolated in pure crystalline form from the adrenal cortex. Many of these are active physiologically. But it was found that there always remained a residue which could not be crystallized, but which, when tested on adrenalectomized animals, had a higher biological activity than the crystalline substances. In 1952 Simpson, Tait and their colleagues, whose work was referred to in our issue of April 21, 1956, detected biologically and isolated chromatographically, from the amorphous fraction of adrenal extract, something which caused intense retention of sodium and diuresis of potassium in adrenalectomized rats. The effect of this substance on sodium metabolism was thirty times greater and on potassium diuresis three times greater than that of desoxycorticosterone; it was first given the name of electrosterone. The substance was soon isolated in pure crystalline form and its constitution determined; in 1955 it was synthesized. Its chemical structure is like that of corticosterone, but the CH_3 attached to carbon 18 is replaced by a CHO group, hence the present name, aldosterone. J. W. Conn, who has done a great deal of work on the clinical aspects of aldosterone, also mentioned in the issue of April 21, 1956, has reviewed the present and possible future position of aldosterone in clinical medicine.[1] Cortisone and hydrocortisone used for substitution therapy in Addison's disease lacked the capacity to maintain normal metabolism of sodium and potassium. Desoxycorticosterone, an artificial hormone not found in the adrenal cortex, had to be given. Corticosterone was found to provide, in a single compound, good replacement therapy. Conn showed that the concentrations of sodium and chloride of thermal sweat could be used as an index of the activity of endogenously produced "desoxysterone-like" or "salt active" corticosteroids. This index has been very useful in clinical investigations. He found that under conditions of sodium deprivation in man, the adrenals are capable of maintaining for long periods of time an excessive output of desoxycorticosterone-like steroids. It was found that the steroid produced in excess was aldosterone. Whenever a reduction of sodium in the diet takes place there is increased secretion of aldosterone. Patients with panhypopituitarism were found to produce almost normal quantities of aldosterone while patients with Addison's disease produced much less or none. The secretion of aldosterone does not seem to be under the control of ACTH or the pituitary. After surgical operations a greatly increased secretion of aldosterone takes place. Conn has shown that many pathological conditions are associated with increased aldosterone secretion. Among these are nephrosis, congestive cardiac failure, cirrhosis of the liver and eclampsia. In all these conditions the aldosterone is excreted in the urine. Deficiency of aldosterone secretion is not yet known except in Addison's disease. How aldosterone secretion is controlled is not known, but it must be by a non-pituitary stimulator, for removal of the pituitary produces only a minor decrease in the secretion. Since nothing is as yet known of this there is no known treatment for excess secretion, and the increased secretion in the conditions noted is probably compensatory and designed to overcome a biochemical abnormality. There is, however, one condition of increased secretion in which treatment can be satisfactory. This is the condition of

[1] *Arch. Int. Med.*, February, 1956.

primary aldosteronism described by Conn[1] in 1955. The cause of this is an aldosterone-secreting adrenal cortex adenoma. In the short period since its description at least 30 cases have been noted and in ten of these an adrenal cortex tumour has been demonstrated. One case has been described from Brisbane.

The major clinical manifestations of the syndrome consist of periodic severe muscular weakness, intermittent tetany and paræsthesia, polyuria and polydipsia and arterial hypertension. The characteristic biochemical changes are reduction of potassium, increase of sodium in the blood, and alkalosis. An interesting point is that very large doses of potassium have only very slight effects on the levels of potassium in the blood. There is no change in organic metabolism. There is a great excess in intracellular sodium in the muscles and a great deficiency of intracellular potassium. The condition clears up completely in about two weeks after removal of the adenoma. When aldosterone becomes available for clinical use it will be valuable, in proper combination with hydrocortisone, in replacement treatment of Addison's disease.

CARDIOMIMESIS.

THE term cardiomimesis has been coined as a name for that condition of imitation heart disease which, by the misinterpretation of real or imaginary symptoms, gives rise to anxiety and confusion in patients and relatives and forces the medical practitioner into the thorny path of proving to, and persuading, them that no organic heart disease is present. P. C. Gibson[2] suggests that mimicry and pretence are natural tendencies in the adult; the suppression of obvious fear finds other methods of expression such as reflex inhibition by fainting. In imaginative people the response to fear increases in complexity and is readily organized into the imitation of organic heart disease. Particularly during the first World War the so-called effort syndrome is reported to have accounted for 44,000 disablement pensions. The syndrome was much less common in the second World War, probably owing to the more careful grading and distribution of manpower. Gibson suggests that pain around the heart is too often misinterpreted as of anginal origin and that it is easy to be deceived by symptoms such as chest pain, breathlessness, palpitation and faintness which can be easily imitated. Breathing, being partly voluntary, may be affected by neurosis, though the breathless hysteric experiences no difficulty in relating his symptoms and makes no effort to conserve his breath. Palpitation of nervous origin has not usually the abrupt onset and termination of true paroxysmal tachycardia which is more unpredictable. Simple tachycardia calls for further investigation and digitalis mistakenly given for this may give rise to extrasystoles which themselves give rise to cardiac neurosis.

Angina is pain referred throughout the nervous supply extending from the second cervical to the lower middle thoracic segments. As this includes the area of all the thoracic organs and structures, the distribution of the pain in itself is of little help in the differential diagnosis. More important are the quality of the pain and its response to effort and to drugs. Pain tends to follow familiar pathways, so that left shoulder-arm pain appears to be a recurrence of previous myocardial ischæmia or of previous local shoulder arthritis when in fact the opposite condition has arisen. The apparent persistence of pain after myocardial infarction may not infrequently be due to lesions at the head of the humerus. Visceral pain may be even more difficult to differentiate. The pain of gall-stone colic may have the same character and segmental distribution as angina; though the pulse rate may be slow, there is no shock, and instinctively the patient moves about to relieve the pain especially by the dispersion of attendant flatulence and by vomiting.

The post-gastrectomy dumping syndrome can mimic coronary thrombosis, though the surgical history, the rapid recovery, and the previous attacks related to meals help in the diagnosis. The pain of hiatus hernia is again similar but is related to meals and posture. The splenic flexure syndrome causes similar pain relieved by the expulsion of fæces or flatus. A difficult problem in differentiating the cause of pain may arise after pulmonary embolism, though the history, the signs of venous congestion and the electrocardiographic findings should help in diagnosis. Women at the menopause sometimes complain of left submammary radiating pain with no clear-cut relation with exertion, occurring at night, associated with vasomotor instability and relieved by sedation rather than by vasodilators. However, even the pain of true angina is not always related so precisely to effort as that of intermittent claudication. Factors such as the state of the weather, the state of the digestive system and the psychological make-up of the patient vary in their symptomatic response to myocardial ischæmia. Gibson concludes that the classical cardiac symptoms are each a process rather than a state, because they are essentially dynamic and are brought about by the fear of sudden death. Thus it is important in the treatment of both organic and functional heart disease to eliminate fear. Gibson holds that psychiatry may well play a larger part than it does in the treatment of heart disease, though an effective substitute for fear calls for the new dynamic and new directive approach of religious convictions.

[1] *J. Lab. & Clin. Med.*, January, 1955.
[2] *Practitioner*, March, 1956.

THE MEDICAL RESEARCH COUNCIL OF NEW ZEALAND.

THE Medical Research Council of New Zealand has issued an illustrated brochure, presumably in order to attract funds, since its last article deals with the problems of finance. It is, however, full of information of which the average practitioner in Australia is not, but should be, aware. In December, 1937, an attempt was made to put medical research in New Zealand on a properly coordinated and organized basis. A Medical Research Council was established as a departmental committee under the Minister of Health and this body continued to function until March, 1951. In 1950 the *Medical Research Council Act* was passed by Parliament and the new Council came into being in April, 1951. The Council consists of three ex-officio members, the Director-General of Health, the Permanent Secretary of the Department of Industrial Research, and the Dean of the Faculty of Medicine of the University of Otago. There are also two members nominated by the Senate of the University of New Zealand and one member each from the New Zealand Branch of the British Medical Association, the Board of Health, the New Zealand Committee of the Royal Australasian College of Surgeons, and the Royal Society of New Zealand. One wonders why the authorities have denied themselves the benefit that would come from inclusion of a representative of The Royal Australasian College of Physicians.

The work of the New Zealand Medical Research Council is organized under special committees which deal with selected problems within their scope. The actual work is reviewed twice a year by the Council and "changes in method and approach are made as required". Financial grants are made to each of the committees according to their requirements from the annual grant-in-aid from the Government. The committees are: "Clinical Medicine", "Dental Disease", "Nutrition", "Microbiology", "Endocrinology", "Neuropathology and Neurophysiology", "Obstetrics", "Chest Diseases", "Surgery", "Island Territories", "Toxicology". The brochure has sections dealing with these committees, most of them with pictures showing heads of the departments at work. The annual grant-in-aid is at present £55,000. The brochure ends with an appeal for funds. That is probably why there is no list of published works; this presumably appears with the annual report.

Abstracts from Medical Literature.

PATHOLOGY.

Aneurysms of the Aorta.

P. BRINDLEY AND V. A. STEMBRIDGE (*Am. J. Path.*, January-February, 1956) have studied the incidence and the particular characteristics of aneurysms of the aorta as revealed by the routine post-mortem examination of over 9,000 subjects recorded during a period of sixty-two years. The majority of the cases occurred in the fifth, sixth and seventh decades of life. Aneurysms of the arch of the aorta tended to occur in younger patients, whereas lesions of the abdominal aorta and multiple and dissecting aneurysms were found in older patients. Syphilis was the ætiological agent in over half the cases. Aneurysms were most often saccular and usually involved only one anatomical segment of the aorta. Multiple aneurysms and dissecting aneurysms were present in 11% and 12% of the cases respectively. In over 80% of those subjects in whom a dissecting or abdominal aneurysm was discovered, cardiac hypertrophy was also found. Rupture of the aneurysm was the cause of death in 39% of the cases. A comparative study of the cases recorded at the beginning and at the end of the series indicated an increase in diagnostic acumen, better treatment and a longer natural life span on the basis of the following trends: a decrease in the incidence of aortic aneurysms; an increase in aneurysms involving the abdominal aorta, or both the abdominal and the thoracic aorta; a decrease in aneurysms having syphilis as their ætiology; an increase of aortic aneurysms based upon arteriosclerosis or cystic medical necrosis; an increase in the average age of patients with all types of aortic aneurysm; an increase in the age of patients with syphilitic aneurysms; and a decrease in the average age of patients with arteriosclerotic aneurysms.

Splenic-Gonadal Fusion.

W. G. J. PUTSCHAR AND W. C. MANION (*Am. J. Path.*, January-February, 1956) have surveyed the reported cases of splenic-gonadal fusion and have added four new cases noted by themselves. The anomaly occurs in two forms, allowing division of the cases into two major sub-groups. In the first, there is continuous splenic-gonadal fusion in which a continuous cord-like structure connects the spleen and the gonadal mesonephric structures. In the second, the splenic-gonadal fusion is discontinuous and the fused spleno-gonadal mesonephric structures have lost continuity with the main spleen and appear as a special variant of accessory spleen. Almost invariably the splenic-gonadal fusion involves the left gonad. Most of the cases have been observed in the male subject. Study of this particular malformation in its embryological aspects indicates that the abnormality arises between the fifth and eighth weeks of embryonic life. Defects of the extremities have been observed in combination with splenic-gonadal fusion in five of the 30 reported cases, and in three of these five micrognathia was also found. The authors suggest that this association of rare malformations in almost one-fifth of the series constitutes evidence of a syndrome, since it occurs in too high a proportion of cases to be an effect of chance.

The Thoracic Duct in Malignant Disease.

J. M. YOUNG (*Am. J. Path.*, March-April, 1956) has dissected out the entire thoracic duct, its main tributaries, draining nodes, and left supraclavicular nodes, during the examination of 150 consecutive subjects in whom death was caused by malignant disease, excluding tumours of the brain and of the blood-forming system. The thoracic duct was found to be involved in over one-third of the cases of carcinoma and over two-thirds of the cases of lymphoma. The left supraclavicular nodes contained tumour in similar proportions in the cases of carcinoma and lymphoma respectively. The lymphoma involved the thoracic duct almost entirely by direct invasion through the wall. Carcinoma was found to spread principally through its radicles, but direct invasions occurred with the adjacent carcinomata of the œsophagus and of the bronchus. Frequently the involved Virchow's nodes were not palpable. From this, the author suggests that involvement of the thoracic duct and of the left supraclavicular lymph nodes must be by no means unusual, so that biopsy of the nodes, even when they are not palpable, should be performed more frequently to help to establish a diagnosis of intraabdominal or intrathoracic disease. It would appear that the thoracic duct is a very frequent and important pathway for the dissemination of neoplastic disease.

Dextran in the Tissues.

A. L. VICKERY (*Am. J. Path.*, March-April, 1956) has studied the fate of dextran in the tissues of the acutely wounded. In the study of battle casualties in Korea the histological localization of dextran was made by a modified periodic acid-Schiff staining method; the aqueous solubility and relative alcohol insolubility of dextran molecules as basic features of the technique were used. Dextran-staining material appeared rapidly in the human kidney and could be demonstrated in all portions of the nephron. Intracellular granules identified as dextran have been observed in the proximal convoluted tubules of man and of experimental rats, and the author suggests that this mechanism is related to dextran absorption or metabolism. Granules of dextran-staining substance were noted occasionally in the reticuloendothelial cells of human liver and spleen, but these were too minute and scattered for interpretation. However, in the rat tissues definite and distinct focal phagocytosis was evident. The appearance of dextran material within hepatic cells apparently occurs soon after infusion and probably is associated with the metabolic breakdown of the dextran molecules in this organ. Vickery found that there was scant evidence of the diffusibility of dextran into tissue spaces except in association with abnormal physiological states. Specific instances of the latter are cited and include dextran immobilized in the pulmonary œdema fluid of shocked patients and in the skin tissues of the severely burned. Swelling of renal convoluted tubular cells was noted to be a constant sequel of dextran therapy. This swelling was correlated with intracellular dextran in the histochemical preparations. These changes were morphologically similar to those following hypertonic sugar infusions and appeared to be non-toxic and transient. Four of 15 patients who subsequently died had symptoms of anuria and presented the pathological findings of lower nephron nephrosis. The nephrosis-like tubular changes observed in kidneys following the administration of dextran were present consistently, and in some cases were striking. The tubular changes were not associated with any cellular response or recognizable signs of local tissue reaction. They appeared to be transient and reversible. None of the tissues studied showed any recognizable lesions referable to dextran toxicity.

Pathology of the Prostatic Median Bar.

B. G. CLARKE AND R. LATOURAGA (*Arch. Path.*, January, 1956) have made a histological and clinical study of 17 patients with a prostatic median bar treated by transurethral resection. The predominant lesion proved to be a thickened, firm, raised internal sphincter composed of hypertrophied, smooth muscle fibres and bundles. The hypertrophied smooth muscle fibres almost invariably showed perinuclear vacuolation, and this was most apparent in the most hypertrophied fibres. There was also œdema of the stroma, which in the severest cases had proceeded to fibrosis. In no instance was there significant histological evidence of an inflammatory process. These changes were not observed in the fibro-muscular stroma of specimens obtained from patients with lobar hyperplasia of the prostate. The best results of the treatment were attained in patients in whom there had been no previous evidence of chronic prostatic infection. The age distribution of the patients and the chronicity of their complaints suggested that in some cases at least the lesion may have been congenital.

Jaundice During Chlorpromazine Therapy.

S. LINDSAY AND R. SKAHEN (*Arch. Path.*, January, 1956) have described the histopathological changes found on biopsy of the liver of five patients who manifested jaundice after therapy with chlorpromazine. The histological appearance of the hepatic tissue observed in each of the biopsies was, in general, similar. Hepatic parenchymal cellular swelling was particularly pronounced in the central third of each hepatic lobule. In the lobules of some livers the central sinusoids appeared to be wider, although empty. Some single hepatic cells were degenerating and were characterized by fragmentation of cellular membranes and nuclear fading or pyknosis. In a few cells

hyaline degeneration of the cytoplasm was present and in other instances individual cells had disappeared. Where the central parenchymal cells were altered the cytoplasm was more granular and coarse. The cytoplasm of the central hepatic cells usually contained granular brown pigment which, unlike the bile masses, stained with fuchsin and was identified as lipofuchsin. Each of the five livers displayed some degree of regenerative activity of the hepatic parenchymal cells, characterized by nuclear pleomorphism, enlargement, and hyperchromatism. The larger nuclei as a rule contained enlarged nucleoli. Mytoses were few. These evidences of regeneration were usually more pronounced in the central portions of the lobules, but were observed peripherally as well. The authors suggest that the hepatic lesion disclosed by biopsy is different and easily distinguishable from that occurring in external biliary obstruction, from various other forms of severe toxic hepatitis, and from cholangiolitic biliary hepatitis or cirrhosis. Cellular injury was mild and reversible and principally centrilobular. Bile stasis was confined to the central biliary canaliculi.

Poliomyelitis and the Spinal Cord.

A. B. BAKER AND S. CORNWELL (*Arch. Path.*, March, 1956) have made a detailed histological study of the entire spinal cord of 50 subjects in whom death was due to bulbar poliomyelitis. The pathological alterations were correlated with the clinical symptoms. Meningeal involvement was found in half of the cases. The meningeal involvement was invariably mild and was usually present in the anterior commissure, often surrounding the spinal vessels. It bore little relation to the inflammatory or neuronal changes within the underlying spinal cord tissues. There was also no correlation between the degree of meningeal change and the clinical manifestations, such as the tightness of the neck and back muscles, or the spinal fluid cell count. All cell groups were damaged in the cases studied, the anterior horn cells, the internuncial cells and the cells of the intermedio-lateral cell columns being the most severely involved. Anterior horn cells were damaged in 43 of the cases, the internuncial cells in 12, and the intermedio-lateral cell column in 15. The cells of the posterior horn and of Clarke's column were involved only in isolated cases, and such involvement appeared to be secondary to the associated severe involvement of the entire spinal cord. Damage to the anterior horn cells correlated fairly well with the degree of muscle weakness. Since the internuncial cells were rarely involved alone, it was impossible to correlate their damage with any type of clinical manifestation.

Lesions of Cartilaginous Joints in Ankylosing Spondylitis.

B. CRUICKSHANK (*J. Bact. & Bact.*, January, 1956) has studied the histological changes occurring in cartilaginous joints of patients with ankylosing spondylitis, on the evidence both of biopsy material and of material obtained at the post-mortem examinations. In the manubrio-sternal joint, the earliest change was found to be one of subacute osteitis followed by the formation of granulation tissue which eventually replaced both the joint structures and the adjacent bone. Later changes were found to be fibrosis of joint and bone, and ossification that progressed to complete synostosis. In the *symphysis pubis* in one of two instances, granulation tissue was found to be replacing the bone and invading the joint; in the other, fibrosis and osteosclerosis were found in one of the pubic bones. In the intervertebral discs, loose vascular fibrous tissue, with little evidence of inflammation, replaced the *nucleus pulposus*, the *annulus fibrosus* and sometimes portions of the adjacent vertebral bodies. Ossification was found to accompany these changes and was the predominant feature in many discs examined. Lateral bony ridges (syndesmophytes) occurred when the ossification was extensive. Hyperplasia of bone also affected portions of the vertebral bodies. The changes in the manubrio-sternal joints and in the *symphysis pubis* closely resembled one another, both histologically and radiographically. The changes in the discs in the later stages were essentially similar to those in the other two joints, although some differences were observed. Identical lesions in the manubrio-sternal joint were found in occasional cases of rheumatoid arthritis, but were not detected in a large series of cases of non-rheumatic disease. The subchondral lesions in the manubrio-sternal joint were believed by the author to be the uniform pattern of reaction of cartilaginous joints affected by inflammatory processes.

MORPHOLOGY.

The Interscapular Gland of the Fruit Bat.

W. A. WIMSATT (*Anat. Rec.*, March, 1955) has studied the interscapular gland of the tropical American fruit bat, *Artibeus jamaicensis*, to settle varying published reports concerning the presence or absence of ducts from this gland. He finds that the interscapular gland is a lobe of the parotid gland and contains normal ducts, and that the brown adipose tissue within the interscapular and cervical fossæ is ductless. The neck of this bat is completely encircled by parotid tissue; Stenson's duct originates from the lateral segment, near the angle of the jaw. There are two pairs of submaxillary glands and a small pair of sublingual glands. *Artibeus jamaicensis* does not have the large, discrete interscapular masses of brown fat described for other genera, but does have smaller sheets and masses around and between the salivary glands and within the connective tissue of the parotid glands.

Sensory Ganglia of Cranial Nerves.

GWEN HALLEY (*J. Anat.*, April, 1955) reports investigations on the development of the sensory ganglia of the cranial nerves, involving a study of 54 cat embryos ranging from thirteen to twenty-two days' development. She states that the cranial neural crest, in the cat, arises as three distinct masses, the trigeminal, the acoustico-facial and the vago-glossopharyngeal crests. The anterior portion of the trigeminal crest dissociates as mesectoderm, while the posterior portion remains relatively compact and forms the *Anlage* of the trigeminal ganglion. The ectoderm overlying the trigeminal crest becomes placodally active, and nodules and strands of epithelial cells detach from the epidermis and become incorporated within the trigeminal ganglion. The acoustico-facial crest extends as a solid column of cells into the hyoid arch; subsequently many of the crest cells in the epibranchial region degenerate, and the geniculate ganglion appears to arise in large parts from an epibranchial placode. The auditory ganglion arises, in part if not entirely, from the epithelium of the auditory vesicle. The vago-glossopharyngeal crest differentiates into separate glosso-pharyngeal and vagal portions; cells become detached from the distal ends of both vagal and glossopharyngeal crests and appear to contribute to the tissue of the more posterior branchial arches. The glossopharyngeal neural crest separates into superior and petrosal parts, and the petrosal portion fuses with an epithelial mass derived from the epibranchial ectoderm of arch III to form the petrosal ganglion. The vagal neural crest forms separate jugular and nodose portions; the nodose neural crest fuses with the epibranchial ectoderm of the dorso-caudal border of the cervical sinus, and the nodose ganglion arises at the site of this fusion. This epibranchial ectoderm is the placode of the vagus nerve; and represents the fused epibranchial placodes of the more caudal pharyngeal arches. Later, the placode of the vagus becomes submerged beneath the surface ectoderm and soon separates from it as a small vesicle, which eventually loses contact with the nodose ganglion, but remains attached to the dorsum of the third pharyngeal pouch.

Hairs of the Rabbit's Ear.

G. WEDDELL AND W. PALLIE (*J. Anat.*, April, 1955) continue their studies on the innervation of skin with investigations of the number, size and distribution of hairs, hair follicles and orifices from which the hairs emerge, in the rabbit's ear. They find that merely counting the hairs in an area of skin and the myelinated nerve fibres entering this area does not give enough data to determine the role of hairs as sense organs; as many as seven hairs, arising from single follicles, may emerge from a single small orifice in the skin, suggesting that orificial clumps may constitute composite sense organs. Furthermore, these orifices are grouped in discrete clusters in some areas, suggesting that these may constitute larger sense areas. The average number of hairs on one ear is about 100,000 (4% of which have no follicles), of orifices from which they emerge about 40,000, and of clusters of orifices about 13,000. These numbers are not related to the size of the rabbit. The number of hairs on the front of the ear is about half the number on the back, but the numbers of orifices and clusters of orifices is about the same, back and front.

Special Article.

SOCIAL SECURITY IN THE FIELD OF HEALTH CARE: ITS BACKGROUND AND PROSPECTS.

THE following contribution on social security in the field of health care was presented to the ninth session of the World Medical Association at Vienna in 1955 by Dr. Dag Knutson, Chief Physician of the University Polyclinic for Internal Diseases, Karolinska Sjukhuset, Stockholm. It is published with the permission of Dr. Louis Bauer, Secretary-General of the World Medical Association.

Much has been written about the medical profession and its relations to "the outer world"—in particular that part of it which deals with social security, where a great deal falls within the scope of medical activities. What has thus been placed before the eyes of the attentive reader discloses that little love seems to be lost between the profession and those whose calling it is to provide social security and to extend its blessings to ever greater parts of the population through collective means. In only a few countries do these two groups seem to work together in harmony and, especially in so-called advanced countries, produce documents of real value.

In principle doctors are naturally anything but opposed to the idea of social security—it would indeed be remarkable if they were, considering the traditions and tasks of their profession. But, in many ways they find modern trends in its development dangerous and ill advised. These tend to create a bureaucracy and massive administrative machinery, which divert moneys from more practical objectives. They tend to introduce statistical points of view where such are not really applicable, leading to a levelling of benefits which results in too much or too little in relation to highly individual needs. They tend to come between the doctor and his patient, transforming the latter from an individual needing health care to a social mass demanding benefits. They tend to push matters further and further into the political field, thereby introducing alien elements with unexpected consequences and often a departure from sound psychology.

The World Medical Association in its notable "Statement on Medical Aspects of Social Security" draws attention to the fact that all these matters become very complicated for the medical profession: "The success of its work is the result of team-work, where the team consists of two members: the doctor and his patient. Much depends on the cooperation of the latter. Restoration of health to a great extent depends on the will of the patient to get well: this will must be encouraged. If the will is there, doctors can the more easily heal their patients, as well as control the functioning of social security in their own field—both fairly successfully. If it is not, they will probably fail."

Naturally these words—and others to be found in the same statement—were received with mixed feelings. In some places the orthodox Press had convulsions of fury—naturally due to possible political implications, which shows the truth of Dr. Ffrangçon Roberts's words: "Among all the subjects with which governments are concerned, health is in many respects unique. Emotion and sentiment are its natural accretions, of which it can be stripped only with the greatest difficulty, and those attempting the task run the risk of being charged with callousness. It is thus weighted with meretricious party-political value."

The position of "the other side" is perhaps less clear. It expresses itself, at least officially, with a certain caution as to the medical profession—although bitterly critical remarks can be found. In a round-about way we can deduce that doctors are far from popular. They insist upon having a liberal profession. They keep talking about the doctor-patient relationship as a fact which remains uninfluenced by development in the field of social security. They refuse to be looked upon as technicians in the service of institutions, whose role is to safeguard the material welfare of people who have lost the necessary balance, namely health. They insist upon looking at the whole through the individual and they won't cooperate. All this because they have not "adapted themselves to new social forms of organization", nor noticed that "sickness has become a social phenomenon, which affects the whole national economy". As Mr. Lavielle complains: "The language of doctors is getting further and further away from the language of social security."

In voicing these complaints, the social security planners would do well to recall that they have rarely if ever consulted the practising medical profession, and any advice they may have received from the profession has been consistently ignored. No medical care programme can ever be successful unless it has the cooperation of those who have to carry it out. Is it any wonder, then, that the doctors are demanding that they be consulted at the planning level? Perhaps if the doctors were consulted the social security planners would have less difficulty in understanding the language of doctors.

Off and on we are led to suspect that there are, from our point of view, more serious complaints, dealing with medical ethics, personal integrity and proper financial disinterestedness. However, if the language here is cautious, the medical profession should observe the fact, in case there is fire behind the smoke.

One thing, though, is extremely clear—doctors and their activities cost a great deal of money, which is steadily increasing, thus causing social security institutions severe headaches. At the bottom—and this applies to practically all discussions and all statements coming from these quarters—the difficulties and complaints involve unconquerable financial difficulties. Deficits are always threatening, receipts and expenses do not balance and, above all, expenses show an appalling tendency to increase, even where the general standard of living is high and rising—as in most well-developed countries. This is a truth which is openly admitted by the social security institutions themselves, which frantically hunt for ways and means to increase their revenue and to diminish expenditure. The possibilities of increasing revenue are limited by hard and realistic facts, while reducing costs meets a multitude of obstacles, some of which—and important ones—are consequences of that meretricious party-political value, of which Roberts speaks.

Under these circumstances it is understandable that doctors come under consideration by those who have to try to make both ends meet. A very considerable part of the costs of social security go through the hands of the medical profession, which evidently has, in addition to other obligations, been given new and complicated ones. Just how big this part of the cost is cannot be stated. Available statistics do not provide such detailed analysis. The question of how much the medical profession is responsible for costs and their augmentation remains, for the time being, unanswerable. Naturally, even more impossible to learn is whether the profession, through letting itself be too much influenced by patients' wishes, or for other reasons, incurs avoidable expenses and, if so, to what extent. It is, however, highly improbable that the steady and in fact rather frightening increase in social security costs should be attributed to doctors' activities other than those due to the introduction of new or increased benefits and additional strata of the population. Also it must be remembered that many of the social security activities fall entirely outside the scope of medical work.

Some hard facts as to the actual, or at least comparatively actual, situation can be found in "The Cost of Social Security, 1949-1951", recently published by the International Social Security Association in collaboration with the International Labour Organization. The document has been referred to as a source of information of undeniable interest in the Report of the Social Security Committee to the 9th General Assembly. It should be viewed as an attempt to create a basis for international comparison of social security costs. Considering the variety of social welfare systems in use, the incompleteness of national statistical material and the intricacies, which characterize the distribution of sources of income as well as expenditure in the modern community, great caution has to be displayed in using and in interpreting the material. The reader is in fact advised to do so. Many questions are left unanswered. The total costs of social security are not available, as the "national social security system" of each country has had to be limited to certain schemes which satisfy the criteria of being legally established, administered by public, semi-public or autonomous bodies, and intended to provide curative or preventive medical care, means of subsistence or supplementary income. Certainly a great many efforts with similar aims are excluded from the investigation and the total "turnover" of all activities cannot even be estimated. There is, wisely enough, no definition of the expression "social security".

Nevertheless some interesting facts are revealed. Of the eighteen European countries included, seventeen have reported total expenses relative to pertinent social security schemes. In the year 1949 the grand total for these expenses amounted to a sum of 12,715,000,000 U.S. dollars. Two years later the corresponding sum was increased almost 30% or by 4,012,000,000 U.S. dollars—to a total of 16,727,000,000.

Similarly, in 1949-1950, twelve non-European countries together expended 13,460,000,000 U.S. dollars, and in 1951 this

sum had been increased by 1,472,000,000 to a total of 14,932,000,000. The distribution here is more uneven than between the European countries, and the U.S. alone expended about 80% of the mentioned total sum. All in all then, for that part of social security which has been recorded, in 1951, 29 countries spent 31,659,000,000 U.S. dollars, increasing expenditures over 1949-1950 by 5,484,000,000.

The total sums are probably not imposing if compared, for instance, to those spent on armament. Nevertheless they give an overall picture of where we are. They also seem to explain why social security institutions begin to feel disturbed. Perhaps of greater interest are the figures on the increases of expenditures: for European countries in two years about 30% and for all recorded countries about 21%.

Of further interest is the fact that administrative costs in European countries for the year 1951 amount to a grand total of 680,000,000 U.S. dollars. In the U.S.A. alone this was 512,000,000. Data on this type of expenditure are, however, far from complete, many items being too entangled with other expenses to be extricated. It is to be assumed, however, that the sums used for administrative expenses also have increased. The basic tables do not permit comparisons on this item, but the steady depreciation of most currencies with a corresponding increase in wages and prices, on, for instance, paper, would make such an assumption highly probable.

However, trends of development are of greater interest than actual status. Will costs continue to increase at the same rate, and can they do so? If they do so, why?

These questions are, for many reasons, extremely important to the medical profession. A very considerable proportion of social security expenses fall under the two headings "social insurance" and "public health services". Between them they are generally responsible for well over 50% of the expenses, and the main part of doctors' activities as well. Total receipts of social security as reported in this investigation are expressed as percentages of total national income, and range in Europe in 1951, from 7·1 to 20—with one exceptionally low figure: outside Europe they are a bit lower, with a scale varying between 1·6 and 12·6. Thus we see that the recorded activities alone handle sums of such magnitude, that the impact on economic life must be extensive. In reference to its repercussions on "social life", this cannot, of course, even be estimated, unless that term is given a limited and purely material meaning.

This is particularly true of countries, where the general standard of living is highest and it therefore would be expected that *"les enfants de la patrie"* need not ask their Alma Mater to assume so many of their responsibilities for their own social security, which in one way or another are ultimately charged to their own expense.

The answer to the questions just asked is, in all probability, in the affirmative. To quote the President of the Italian National Sickness Insurance Institute: "The accounts of the (social security) institutions will always show a deficit and will constitute a burden until the moment arrives when governments will apply themselves seriously to the problem." Here one might insert the remark that governments certainly seem to apply themselves to the field in question—whether seriously, in the sense desired by Mr. Petrilli, can be left aside for the moment. Most doctors would agree with Mr. Petrilli. They would also agree with the Head of the Legal Division of the Venezuelan Social Insurance Institute, who in discussing factors that influence the costs of social security, especially medical services, states that "where social insurance is in course of progressive application to the whole country, each new extension causes a disproportionate expenditure which may be explained as follows:

"(a) A great part of the beneficiaries in a new zone rush to take advantage of the insurance, with consequent congestion,

"(b) the mortality (morbidity?) index for such a zone is relatively high, and

"(c) the industrial development and the population covered are not sufficient to produce an income to balance the expense. It must also be borne in mind that in districts in which social insurance has been applied for some time, the Institution slowly creates in the beneficiaries the habit of resorting to medical services whenever they feel the slightest physical indisposition."

This statement refers mainly to conditions in Latin America, but seems to be fully applicable to conditions elsewhere. Like Mr. Petrilli, Mr. Ulloa raises "the question of a greater participation by the state in the maintenance of the medical services and the possibility of arriving at a national medical service".

These two highly experienced gentlemen then seem to be of a somewhat pessimistic turn of mind, where the financial prospects of social insurance are concerned. They, as well as the International Association which they represent, feel that, to a considerable extent, doctors should be blamed for this situation. Those of us who have studied the Resolutions of the International Social Security Association on Medical Secrecy, on the Prescription of Medicaments, and on the Conclusions Concerning the Relations Between Social Security Institutions and the Medical Profession, have formed a strong impression of their opinion.

It is for the profession to consider whether its activities in the field of health-care (the possibility of occasional but always deplorable instances of misconduct being recognized) follow not only the rules of science but also those of ethics, in recognition of the fundamental principle that any claim for freedom and authority must be accompanied by a guarantee. It is also the duty of the profession to define its scope and contents. This has, in fact, been done, and the profession seems to feel that on the whole it observes its existence. Whether "the other side" shares this opinion seems doubtful. Mr. Petrilli finds the most probable solution of the financial difficulties in which social security institutions find themselves, in "giving the principles of professional ethics statutory force". This would not indicate that the "reactionary" medical profession is found "reactionary" even in the manifest recognition of principles of venerable age but of a nature disconcerting to the social security institutions.

However, Mr. Petrilli adds as a second part to his solution "a new interpretation of the practice of medicine consistent with the new exigencies of the social period in which the world finds itself today", and this leads to considerations of a different nature. It has already been mentioned that the International Social Security Association reporters, Messrs. Petrilli and Ulloa, suggest increasing state intervention, and they are by no means the first or only ones introducing such eventualities. The International Labour Organization long ago drew attention to "the tendency of loosening up the ties between benefit right and contribution payment, and of creating a public service for the citizenry at large making all care and supplies available at any time and without time limit. . . ." In other words, the whole field of social security including social insurance, which no longer is insurance *sensu strictiori*, is being centralized and pushed into the arms of the state, governed by state policies. The real answer, therefore, to any question pertaining to future developments has to be sought in the political field even if, perhaps, finally and ultimately the relentless financial realities will be one of the deciding factors. So far, political forces have had some elbow room—or believe that they have—and social politics lends itself well to appealing declarations and building-up platforms for party-political, competitive activities, consequently quickly reaching a central position. It is, in fact, as experts have pointed out, being raised from an humbler position to a leading role, changing its former task of correcting conditions to the new one of creating them. The expansion is brought about in the usual way: needs are discovered, given wide publicity, and immediate steps are demanded to meet these needs. This costs money and the pocket of the tax-payer has to be searched anew—a procedure the success of which depends on the probability of accompanying promises of a reasonable return. So far the average man has paid up, proving himself to be credulous, if not gullible. But even if he is not, he has to pay anyway.

This may be all right up to a certain point—that point being when he begins to feel that his protection and the sugar coating do not make up for his restricted and controlled activities. In the so-called highly developed countries this point has been reached or even passed and he reacts, conscious or perhaps more often unconscious of the real trouble, in different ways. Many of these reactions take him to the doctor. Look at the various delinquencies, at statistics of drug-addiction, divorce and crime. Can we say that we have been able to bring man any nearer that complete mental, physical and social well-being which is the proclaimed aim of social security? This question is raised by a famous British psychiatrist who answers himself with at least serious doubt. The psychosomatic troubles are becoming more frequent, and not only because we have come to observe them more closely.

This then is important. It also means that the doctor's particular section of social security is being drawn into the

political field. For instance, it is extremely misleading to state, as has been done in the International Social Security Association report on Relations Between the Social Security Institutions and the Medical Profession, that the introduction of a compulsory sickness insurance in Sweden with some direct benefits, indicates that the new system would be more advantageous from the viewpoint of the insured and the medical profession. In fact, large numbers of the insured were opposed or doubtful, and the doctors fought the plans from the very beginning, having studied similar systems and their effect in other countries. The matter was more or less purely political, cherished by competing political parties, and left a number of unsolved but important details, and an equal amount of general difficulty for patients as well as doctors. The promise, therefore, to provide the necessary, adequate and most effective medical care for all persons protected becomes a political one. Strengthened and reinforced by article 25 of the Declaration of Human Rights, its scope gradually widens. It tends to be the conception of society's acceptance of the responsibility for man's well-being, that is, his feeling well. The most effective medical care is evidently the one leading to *restitutio ad integrum*, as doctors say. Hence the duty of society goes further and delves into regions of unlimited and still partly unknown areas. Health itself is being raised to the august level of one of Man's Inalienable Rights, the guarding of which eventually becomes a correspondingly important duty of society.

It is essentially here that the views of the medical profession become irreconcilable with those of the social security institutions or their various sponsors, namely, a state, community, ultimately the politicians, generally lay people. At the very foundation is a difference between the lay and the professional conception of health. Health to the laity, beside being something positively good, embedded in emotions and endowed with almost mysterious properties, is often more or less equal to a capacity for work. Often, too, it seems that its production is regarded as a result of comparatively simple and technical measures—the doctor is a technician. The Lima Medical Declaration of 1949 recommends that "systems of evaluation should be worked out among the Social Insurance Assistance Organizations . . . which would evaluate the work of the doctor on the basis of efficiency, rapidity and economy of the diagnosis and treatment of the cases and not merely be based on the number of consultations, operations and medical acts performed". The first part of this recommendation does not sound or promise well—the second part may aim at a mitigation. Finally, the often heard thesis on the enormous gains of modern medicine seems to be interpreted as a promise of immediate practical results.

Not so to the medical profession, for whom health is a state of normal psycho-physical functioning—the neutral point around which the human being revolves and to which he tries to return. Homœostasis, chiefly promoted by inherent propensities, can sometimes be brought about by medical measures. Individual reactions to these are about as numerous as the individuals themselves, and, what makes things worse, somatic factors are increasingly mixed with psychological ones, with even more diversity. Modern society breeds nervous disorders. The craving for higher standards of living through increased production; work under contract pressures; the monotony of factory work in industry; the impossibility of feeling a personal responsibility in the final product of the large industry; the heavy taxation, and the sneaking feeling that the return is not good enough nor the money earned of stable value, and added to this, controlling measures, forms and slow progress when the welfare machinery, so efficient-looking on paper, starts grinding—all of this leaves obvious marks on the mind of the average man, and the doctors of the world can bear witness to this fact. I am aware that I speak as a member of a highly developed society, one of those which are held up as desirable examples for so-called under-developed, non-industrialized countries where "progress" is slow or even imperceptible, but I can frankly state that the tasks of my colleagues and myself are becoming steadily more difficult to fulfil. Health cannot be manufactured. Furthermore, there is no Royal Road to Health. Health is not a reward for faithful abiding by certain rules of living, nor does it exist in proportion to material conditions beyond a rather primitive level.

Finally, in health there is a very definite element of recognition and will, which further contributes to its personal character. Its creation is an adventurous task, for the fulfilment of which medical science, artistic touch, didactic activities and, often, time itself, must join forces. But science means new questions; art moves in the lofty regions of intuition; and the outcome of teaching depends on the quality of the teacher-student team. Hence there are many variables and unknown factors in the equation.

Therefore, if social politics and emanating from it, social security schemes, try to shoulder the responsibility for the well-being of man, there can only be one outcome: demands will forever exceed supply and financial resources. Doctors, whether members of a liberal profession or working as civil servants, whether assuming the role of guardians of the patient or that of controller on behalf of the security system, can do but little to change this, at least as long as they are true to their professional and ethical standards. It is, of course, nonsense to talk about cheap and yet first-class medical care. In view of what has been said, and a great deal which time does not permit me to say, medicine cannot be cheap, and will become less so. He who embarks upon social security schemes including health care at a first-rate level will have to realize that on the whole hopes for a compatibility with available financial resources should be abandoned.

This should not be regarded as a *non-possumus* from those who try to make their fellow man healthier. Nor does it contain an evaluation of any specific system. The medical profession should recognize its heavy responsibilities, scientifically and ethically, and I should like to emphasize each of these with the same force. The medical profession should also cooperate with those whose task it is to see that the doctor's recommendations can be implemented. However, it must demand that medicine not be looked upon as a technology; that the care of the individual patient not be deprived of "social" value or nature; and that this care not be interfered with in a way which further complicates already difficult problems. The medical profession must state that medicine, an age-old art merged with a young science, should set its own conditions of practice, with social security systems assisting in the achievement of the ultimate goal.

World Medical Association.

MEETING OF THE COUNCIL.

THE twenty-sixth session of the Council of the World Medical Association was held at Cologne, Germany, on April 29 to May 6, 1956. The following information has been received from the Secretary-General.

Appointments.

Council named the following individuals to fill existing casual vacancies: *President-Elect*, Dr. José A. Bustamante (Cuba), who is Chairman of the Council of the Pan-American Medical Confederation; *Council Member*, Dr. Hector Rodriguez (Chile), who is Secretary of the Chile Medical Association and currently Regional Secretary for Latin America for the World Medical Association.

Medical Education Conference.

The Second World Conference on Medical Education will be held at Chicago, Illinois, United States of America, on August 30 to September 4, 1959. Officers of the conference will be: *President*, Dr. Raymond B. Allen, Chancellor, University of California in Los Angeles, California; *Deputy President*, Dr. Victor Johnson, Director, Resident Training Programme, Mayo Clinic, Rochester, Minnesota.

In addition, the Council coopted Dr. E. L. Turner, Secretary, Council on Medical Education and Hospitals of the American Medical Association, as a member of the Council Committee on Medical Education.

Medical Ethics and Medical Law.

The Council adopted two principles relative to medical ethics and medical law as a result of its own efforts in a joint committee studying the subject of international medical law, and the proposed organization of an International Organization on Medical Ethics and Medical Law with national chapters. This new organization would be composed of sociologists, jurists and philosophers in addition to doctors, and its aim is to codify the principles of medical ethics. These principles are: (i) The same ethical code must govern the doctor in both peace and war. (ii) It is the function of the World Medical Association to formulate any code of international medical law and not the function of laymen even though they be lawyers.

The Council is of the opinion that the World Medical Association should be unalterably opposed to the attempts of outside groups entering a field in which they are not competent.

Secretariat Liaison Conference.

Secretaries and officials of the National Member Medical Associations and the editors of their journals are invited to a meeting at the World Medical Association Secretariat, New York City, on October 19 and 20, 1956. The programme will be planned to facilitate mutual assistance between the Secretariats of the National Medical Associations and the Secretariat of the World Medical Association. The meeting is scheduled to follow immediately the adjourning of the tenth General Assembly and the twenty-eighth Council Session of the World Medical Association in Havana, Cuba. (Tenth General Assembly, October 9 to 15, 1956; twenty-eighth Council Session, October 16 to 17, 1956.)

The Secretariat Liaison Conference is the outgrowth of a meeting held at the World Medical Association Secretariat in New York City, June, 1955, for National Medical Association secretaries. The orientation and discussion proved to be successful, and those who attended the first meeting were of the opinion that it should include additional officers and officials of the member associations and that such conferences should be convened whenever convenient for these people to meet at the New York Secretariat.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE PERSECUTING SPIRIT OF GOVERNOR BLIGH.

[Extract of a letter[1] from D'Arcy Wentworth to the Right Honourable Earl Fitzwilliam.]

New South Wales,
October 17th, 1807.

My Lord,

The many unspeakable favours I have received from your Lordship and the interest you have always had the goodness to take in everything connected with my welfare and advancement makes me feel confident your Lordship will hear with Concern of the very distressing situation in which I am placed by the persecuting spirit of Governor Bligh.

No sooner had that gentleman commenced this Command than he displayed many demonstrations of determined animosity towards me: and put it beyond doubt that he would lose no opportunity to do me all the injury in his power. So beset with danger, it became doubly incumbent upon me to act with watchful prudence: and although it has been my misfortune not to escape the consequences I had so much cause to dread yet I am happy it is in my power to assure your Lordship that every part of my conduct will bear the most rigid examination.

I will not presume to trespass without permission upon your Lordship's patience by entering into a minute detail of the ill usage I have suffered, but being assured that your Lordship will not allow me to be disgraced and ruined without cause I have taken the liberty to enclose herewith a Packet addressed to the Secretary of State. If your Lordship will have the goodness to peruse the papers it contains you will find the clearest testimony that my conduct has been blameless: and when this is proved to your Lordship's satisfaction I feel confident I shall be pardoned for taking the liberty of respectfully entreating that your Lordship will be pleased to cause the Packet to be sent to the Secretary of State in such a manner as may prevent the influence of my Persecutor from operating to my disadvantage, and may secure for me what I most earnestly desire an opportunity fairly to defend myself. This letter is entrusted to the care of a Mr. Williams a very respectable young gentleman who has been a witness of other instances of oppression that I have suffered from Governor Bligh not alluded to in the papers I now send—should your Lordship be inclined to hear the particulars or to make any enquiries on points that I have not clearly explained, he is perfectly qualified to inform you of every circumstance, and at the slightest indication of your Lordship's wishes he will feel honored to attend on your Lordship.

And I beg that your Lordship will believe me to be with the utmost gratitude and Respect, My Lord,

Your Lordship's most devoted and most humble servant,

D. WENTWORTH.

[1] From the original in the Wentworth Papers in the Mitchell Library, Sydney.

Correspondence.

CHEMOTHERAPY OF PULMONARY TUBERCULOSIS IN PATIENTS AT HOME AND AT WORK.

SIR: In an interesting letter (M. J. AUSTRALIA, May 5, 1956) Dr. John Read details some points of criticism of the article entitled "Chemotherapy of Pulmonary Tuberculosis in Patients at Home and at Work" by D. O'Brien and myself (April 14, 1956).

In reporting on investigation of patients treated at home, we had no intention of advocating this procedure as a routine practice. In fact, the use of chemotherapy for the ambulant patient at home was suggested for only a small group of selected patients who had received previous hospital treatment.

Dr. Read has stressed the importance of bed rest and hospital treatment. He implies that our investigation of alternative treatment was unwarranted and may even have been to the detriment of some of the patients.

I would like to take the opportunity of explaining the genesis of the investigation. Rightly or wrongly, the practice of treating patients at home had commenced in a minor way, especially for patients refusing to reenter hospital. It therefore appeared important to evaluate the results obtained by this non-routine treatment. The patients were not treated at home in order to carry out an investigation; on the contrary, they were investigated because they were being treated that way. Full bacteriological facilities were available and two very competent thoracic surgeons visited the clinic regularly. Surgery was found to be contraindicated in a large number of patients and others refused it. Surgery was performed on a number of patients in the series after the period of treatment at home. Dr. Read's remarks concerning drug resistance are well made. The importance of performing drug resistance studies was not fully realized when some of the patients commenced treatment a number of years ago. This was corrected during the later stage of the investigation.

Dr. Read is rather critical of the criteria used for classification of our results. It can be accepted that the final judgement of any form of treatment of tuberculosis has to wait years of observation. This is difficult of practical achievement, and most investigations involving chemotherapy have been assessed initially by measuring progress after a limited period of time.

Provided final judgement is reserved, this appears to be an acceptable approach and was the method employed in our investigation. The criteria were described as stringent within this context, as we excluded clinical and radiological improvement, which, if included, would have made the results appear more favourable.

As Dr. Read considers it unwise to attempt to improve on the bed rest, hospital programme, I would like to emphasize the importance of examining the place of bed rest in the treatment of tuberculosis.

It is not generally realized that it has yet to be proved that bed rest does add to the effectiveness of prolonged adequate chemotherapy. The assumption has been made that the effect of bed rest must supplement the undoubted effect of prolonged chemotherapy, when the two are used together. This need not be true as the following suggests.

> A preliminary report of an evaluation of in-patient ambulatory versus in-patient non-ambulatory treatment undertaken at Fitzsimons Army Hospital reveals that patients on a programme of free ambulation have fared no worse than patients restricted to modified bed rest. Evidently within reason, we can modify the bed rest routine used in the past. (Committee on Chemotherapy of Tuberculosis. Veterans Administration, Newsletter, February 27, 1956.)

Although I agree with Dr. Read that it would be unwise as yet to abandon the routine use of bed rest, I cannot agree that this practice should be free from investigation. Rather, I submit that it requires to be determined whether bed rest increases at all the effectiveness of adequate chemotherapy, and if it does, for which type of case. This was one reason for our investigation.

In our paper, it was emphasized that only tentative conclusions could be drawn from the results, as there was no comparable control series treated in a contrasting manner. Twenty-eight of our 75 patients were chronic cases with cavitation which had been present, despite previous hospital treatment, for more than one year. This alone made our series likely to compare unfavourably with patients newly admitted to hospital. It would have been entirely fallacious and unscientific to compare our results with those obtained by other authors on patients treated in hospital.

Quite apart from the question of bed rest, domiciliary treatment does have disadvantages compared with sanatorium treatment. Administration of drugs is likely to be less regular and toxic effects are less easily controlled. Also adequate segregation of an infectious patient is not achieved, and education and rehabilitation are harder to arrange.

For these reasons, sanatorium treatment is still preferable to domiciliary treatment for the vast majority of patients.

However, for a small minority of selected patients, without cavitation, chemotherapy at home may be justified.

Yours, etc.,

Repatriation Sanatorium, Kenmore, New South Wales. ALASTAIR H. CAMPBELL.

June 5, 1956.

CHILDHOOD SCHIZOPHRENIA.

SIR: Both Dr. Adey and Dr. McCluskie have confined their criticism of my remarks to the one word "delirium" and have used it to condemn the whole article. This is in line with present-day psychiatric thought, which concentrates on one particular symptom and forgets "the sum total of the personality".

In my criticism of Dr. Williams's article, I pointed out that the word "schizophrenia" was coined as a substitute for the disease *dementia præcox*, which had a definite clinical entity and a complex symptomatology. But schizophrenia, on the other hand, is a term used for a symptom, withdrawal, which is all-important. No matter what the cause of the withdrawal is, if the patient has it, he must be classified as a schizophrenic.

All that the term schizophrenia did was to expand enormously the field covered by the term *dementia præcox*. Hence the unrealistic terminology of today: schizoid personality, acute schizophrenic episodes, schizophrenia, pseudo-neurotic schizophrenia. Little diagnostic acumen is needed to make such diagnoses. If, for example, a patient is confused, restless, noisy and hallucinated, and recovers, it is easy to say that he has had an acute schizophrenic reaction and be content. But psychiatrists trained in an older school would diagnose such cases as examples of delirium or confusional psychosis, and would be anxious to find out the physical cause of the condition. In other words, to them, the psychiatric symptoms present are but a complication of a bodily or neurological condition, and the prognosis is that of the causative disease. If delirium is a "lonely clinical sign", it is a valuable direction to seek a bodily and not a mental cause.

And surely the cases cited by Dr. Williams, and especially those with neurological signs and symptoms, must indicate some underlying neurological or physical cause for their condition. It is too easy to classify them as cases of schizophrenia.

I once worked for eight years in mental hospitals for young children. There I saw clinical conditions on all fours with the cases described by Dr. Williams. The experience convinced me how little we know clinically of these conditions. Amongst them were syndromes not described in text-books and rare neurological conditions. But I did not come across any case I would diagnose as childhood schizophrenia, and Dr. McCluskie himself points out how rare the condition is. Of 20 cases diagnosed as childhood schizophrenia, Seelig could confirm the diagnosis in only four.

Dr. Adey insists on the necessity of correct diagnosis. That is a *sine qua non*. But it is my contention that the diagnosis of childhood schizophrenia is a description of a symptom and not a disease, and by using it we are erecting a smoke-screen to blind us to the true underlying causes.

Yours, etc.,

S. J. MINOGUE.

195 Macquarie Street, Sydney,

May 30, 1956.

"POLIO."

SIR: Dr. Duhig (M. J. AUSTRALIA, June 2, 1956) curses the above term as an "imprecise" (though I find it unambiguous), "slipshod" (though it follows many well-respected precedents), "barbarism" (though the English language is rooted, nurtured and flourishing in barbarisms). Does he loathe the doctor who says "phone" for "telephone", "mike" for "microscope"? Is that doctor's work thereby bound to be more slipshod than Dr. Duhig's, who says "fivers" for five-pound notes?

Semantic confusion is more damnable than established colloquialisms. Dr. Duhig's thinking is inclined to generalize, and may thereby evade the main issue. Does he know that all "disc jockeys" on the "A.B.C." say "pole-io" for "poll-io"? Most of my patients do not. Is he sure that you are our last citadel of precision and taste? If so, what is "Granny Herald" doing about such things?

I expect our worthy colleague injects his venom with tongue in cheek, so in returning it I will rub it in with his own parting shot: "Our dignity and taste should be above such derelict habits of thought and speech."

Yours, etc.,

D. N. EVERINGHAM.

P.O. Box 328, Rockhampton, Queensland.

June 4, 1956.

SCHISTOSOME DERMATITIS.

SIR: In the report (May 26, page 897) of a scientific meeting of the South Australian Branch of the British Medical Association held on September 29, 1955, it is stated that the host for cercariæ producing schistosome dermatitis is *Lenameria pyrimidata*. This is not at all likely. I have examined hundreds of this species, which is very common along the Murray River, without finding any dermatitis-producing cercariæ. The common host is *Limnæa lessoni*. This is a rarer snail, with a more restricted distribution than Lenameria. The snails may be distinguished by two features. Limnæa is right-handed and Lenameria left-handed in the direction of the spiral. And Limnæa is a soft yellow-grey creature, compared with the hard black-red Lenameria.

Fresh-water schistosome cercariæ have been found in the Murrumbidgee swamps and at Boonah near Brisbane as well as in the Murray. They probably also occur in the swamps off the Flinders River in the Gulf country, since men wading the swamps on horseback report papular lesions on their legs.

It may be useful to mention that 30% dimethylphthalate in a lanoline base gives protection to bathers in infested waters.

Yours, etc.,

W. V. MACFARLANE, Professor of Physiology.

Department of Physiology, University of Queensland,

June 5, 1956.

AXILLARY ODOUR.

SIR: Your article (M. J. AUSTRALIA, June 2, 1956) contains the statement: "Certainly above all human olfactory threshold levels the human odours are regarded with extreme distaste." It would be improper for your readers to believe this view is universally held. In support of this claim I would reproduce a footnote from "Applied Physiology" (Ninth Edition), page 467, by the late Samson Wright:

Yas Kuno's views on the functions of axillary sweat are interesting, even if they may fail to command general assent. The following is an undistorted summary of his writings. The axillary sweat smells most strongly and peculiarly and is "superior in attractive power to the scent of the sexual organs or of any other parts of the body". It has developed especially in man because owing to the erect posture scents from the sexual organs or from any of the lower parts of the body are not usually perceptible. The axilla is advantageously placed, and so its scent can act more effectively. If it be true that axillary scent has an attraction for the other sex, then the fact that it is suddenly discharged in emotional states becomes of great significance. The scented vapour would be retained in the axilla and be disseminated occasionally when the arms were moved, and would not be dissipated rapidly as elsewhere. (The phrasing in the above passage is mainly Kuno's.)

Yours, etc.,

A. C. THOMSON.

Sydney,
June 5, 1956.

ALCOHOLISM—A COMMUNITY RESPONSIBILITY.

SIR: The letter in your edition of May 5 from Dr. S. J. Minogue—"Alcoholism—A Community Responsibility"—and the subsequent article in *The Sydney Morning Herald*—"Alcoholic No Case for Psychiatrist"—prompt me, as secretary of the South Australian State Committee on Alcoholism, affiliated with the American National Committee, to suggest that possible misunderstandings about the institutional treatment of alcoholics might arise from Dr. Minogue's letter.

The chairman of my committee, who is also acting superintendent of Northfield Mental Hospital, has a State-wide reputation for the in-treatment of alcoholics in his mental hospital, a long waiting list for voluntary admission, and the confidence of magistrates and probation officers in this State, who are sending to his care many cases who might otherwise remain in gaol. Dr. W. F. Salter recently addressed the South Australian Institute of Psychiatrists on the treatment obtaining at Northfield, and with the heavy incidence of this cause of admissions to our receiving homes, I believe that Dr. Salter's paper would cast a rather different light on the possibilities of the position.

Yours, etc.,

BARBARA K. HEASLIP,
Secretary, State Committee on Alcoholism.

27 Park Road,
Kensington Park,
South Australia.
Undated.

THE MANAGEMENT OF PORTAL HYPERTENSION WITH SPECIAL REFERENCE TO BLEEDING ŒSOPHAGEAL VARICES.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of June 2, 1956, Dr. Blackburn gives an excellent review of the problems confronting the physician in the management of portal hypertension, and reports the results of the therapeutic plan used by his team.

However, I feel that he undervalues the operation of early transthoracic, transœsophageal ligation of bleeding varices advocated by Linton (1953). Injection of the varices with a sclerosing fluid, via the œsophagoscope, after the patient has settled down on balloon tamponage is claimed to be a more desirable manœuvre, and a stepping stone to definitive portal-systemic shunt.

However, Welch (personal communication) has found this manœuvre to be more difficult and less certain that open operation, and furthermore it is inapplicable in the patient who fails to settle down on tamponage—this method of control being by no means certain. The further complication of aspiration pneumonia during prolonged tamponage is a real one, in spite of careful pharyngeal suction. Welch has now abandoned tamponage, favouring immediate ligation of bleeding varices with balloon trial. He feels this will substantially improve the immediate prognosis, for even after successful tamponage and following special diets one is not assured that further bleeding will not ensue. It is known that post-hæmorrhagic improvement in the condition of patients does not of necessity mean a fall in portal pressure (Kelty, Baggenstoss and Butt, 1950), which may actually increase along with improving hepatic function, as regeneration of liver lobules and repair of the cirrhotic liver may increase portal vein obstruction.

The question of prophylactic surgery in patients with liver cirrhosis and proven œsophageal varices is far from settled, but the fact remains that the mortality from bleeding œsophageal varices in cirrhosis of the liver is an exceptionally high one, and warrants a vigorous therapeutic programme.

Yours, etc.,

T. S. REEVE.

82 Stella Street,
Collaroy Plateau,
New South Wales.
June 13, 1956.

References.

KELTY, R. H., BAGGENSTOSS, A. H., and BUTT, H. R. (1950), "Relation of Regenerated Hepatic Nodule to Vascular Bed in Cirrhosis", *Proc. Staff Meet., Mayo Clin.*, 25 : 17.

LINTON, R. R. (1953), "The Emergency and Definitive Treatment of Bleeding Œsophageal Varices", *Gastroenterology*, 24 : 1.

THE NEW SOUTH WALES MEDICAL BOARD.

SIR: It is clear from Dr. Cotter Harvey's letter in your issue of June 16 that the Medical Board's offensive circulars stemmed from two old errors: firstly, mistaking the letter for the spirit; secondly, forgetting that sometimes powers are best left unused.

There is a hierarchy among laws. The great precepts of the natural law bind always. But there are lesser laws, and these include man-made regulations. Some of these (such as the one forbidding surf-bathing at Manly) are better left uninvoked. Others, such as Section 27 and parts of Section 15 of the *Medical Practitioners Act*, should be invoked only to meet special cases. For example, the people may flock, for their surgery, to registered practitioners with a B.A. I know no better example. Perhaps Dr. Harvey could supply some, and explain how such isolated examples (if any) can justify the sweeping circular.

The great principle stands, that "it pertains to the essence of law, that it be reasonable".

Yours, etc.,

V. J. KINSELLA.

235 Macquarie Street,
Sydney,
June 16, 1956.

Obituary.

WILLIAM LOVE KIRKWOOD.

WE have received from Dr. E. S. Stuckey the following appreciation of the late Dr. William Love Kirkwood.

It was my good fortune, about twenty years ago, to serve for some nine months as assistant to Dr. W. L. Kirkwood at Epping. Since that time our friendship has been reinforced by contact from time to time. "W.L." remained in general practice in the same area until his death, and has been for many years the grand old man of his profession—known and loved by a wide circle of grateful patients, fellow practitioners and prominent citizens in all walks of life and of all faiths.

A man of absolute integrity, honest in all his dealings with his fellow man, compassionate towards the frailties of others, constantly striving after the best in the treatment of his patients, and eager at all times to keep abreast of all the advances which have taken place in medicine throughout his many years of devoted service, he has remained in my estimation the ideal of what a general practitioner should be. I am sure that he has been an inspiration to many younger members of the profession who have come in contact with him, and that they have been the better in their dealings with their own patients and with their fellow practitioners because of his example. Those of us who attended his funeral service cannot fail to have felt

that the people in the crowded church were largely those who had regarded him as their "beloved physician". It was characteristic of Kirkwood that, when the call came to him in middle age to serve his country for a second time in military service, he should cheerfully sever all his ties in order to manage a general hospital with diligence, discipline and distinction—and I know that this service was done at considerable financial loss and with detriment to his health.

We who have had the privilege of knowing him are the poorer for his passing; but we are the richer for his influence, which will continue to live, and will in turn, through us, influence other members of our profession.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Course at Wollongong.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the South-Eastern Medical Association, the course at Wollongong this year will consist of three separate evening lectures to be given at the Wollongong General Hospital, as follows: Tuesday, July 10, at 8 p.m.: "Backache and Sciatica", Dr. Selwyn Nelson. Wednesday, July 18, at 8 p.m.: (*a*) "Freedom and Insanity", (*b*) "Murder and Schizophrenia", Dr. E. A. Marsden. Thursday, July 26, at 8 p.m.: (*a*) "The Use and Abuse of Steroid Hormones in Dermatology", (*b*) "The Treatment of Common Dermatoses", Dr. E. J. C. Molesworth.

The fee for attendance at these three lectures will be £1 11s. 6d., and those wishing to enrol are requested to make early application to Dr. John Maloney, 61 Market Street, Wollongong. Telephone: Wollongong B 2496.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 23, of May 17, 1956, and Number 27, of May 31, 1956.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 1/61802 Captain J. Brieni is confirmed.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/127043 Honorary Captain A. R. Doutreband is appointed from the Reserve of Officers, and to be Captain (provisionally), 16th February, 1956. To be Major, 4th April, 1956: 2/79012 Captain (Temporary Major) G. Clifton-Smith.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/35254 Major R. A. Isenstein is placed upon the Retired List (Central Command), with permission to retain his rank and wear the prescribed uniform, 24th April, 1956.

Western Command.

Royal Australian Army Medical Corps (Medical).—5/26523 Captain G. R. A. Raad is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Western Command), 9th April, 1956.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Tasmania Command.—Honorary Captain T. R. Gaha is retired, 13th January, 1956.

Retired List.

The following officer is placed upon the Retired List (Tasmania Command) with permission to retain his rank and wear the prescribed uniform, 13th January, 1956.

Royal Australian Army Medical Corps.

Tasmania Command.—Major D. W. L. Parker, O.B.E.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Appointment.—Roger George Congdon is appointed Surgeon Lieutenant (for Short Service) (on probation), dated 10th April, 1956.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointment.—Eugene Peter O'Sullivan is appointed Surgeon Lieutenant, dated 10th February, 1956.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps.

To be Temporary Major, 18th April, 1956.—1/8072 Captain F. R. Wilson.

Regular Army Special Reserve.

Royal Australian Army Medical Corps.

To be Lieutenant, 21st March, 1956.—SX700106 Vyautas Peter Dainius.

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/251120 Captain C. R. B. Richards is appointed from the Reserve of Officers, 20th March, 1956. To be Captain (provisionally), 30th April, 1956; 2/79217 Richard William Tinsley.

Southern Command.

Royal Australian Army Medical Corps (Medical).—5/20465 Captain G. I. Howard is appointed from the Reserve of Officers, 1st March, 1956.

Western Command.

Royal Australian Army Medical Corps (Medical).—The following officers relinquish the provisional rank of Captain and are transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Western Command), and are granted the honorary rank of Captain: Captains (provisionally) 5/26521 M. C. Smith, 1st March, 1956, and 5/21605 M. C. Canning, 1st May, 1956. The provisional appointments of the following officers are terminated: Captains 5/26527 D. G. Kermode, 17th December, 1955, 5/45805 P. E. Hurst, 12th January, 1956, and 5/32269 J. B. O'Brien, 29th January, 1956. To be Captains (provisionally): 5/26527 Denis Graham Kermode, 18th December, 1955, 5/45805 Peter Edwin Hurst, 13th January, 1956, and 5/32269 John Bernard O'Brien, 30th January, 1956.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Southern Command.—To be Honorary Captains: Brian Alexander Rodan, 13th February, 1956, and Graham Willoby Morgan, 12th March, 1956.

Congresses.

FOURTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST.

THE American College of Chest Physicians announces that the fourth International Congress on Diseases of the Chest will be held at Cologne, Germany, from August 19 to 23, 1956, under the patronage of the Federal Chancellor, Dr. Konrad Adenauer. The scientific programme includes the following subjects: coronary diseases of the chest; industrial diseases of the chest; virulence and resistance under

chemotherapy of pulmonary tuberculosis; pulmonary function; cardiac function; tumours of the mediastinum. There will be panel discussions. The languages used will be English, French, Spanish and German, with simultaneous translation. Further information may be obtained from the Secretariat of the Fourth International Congress of the American College of Chest Physicians, Köln-Deutz, Messeplatz (Germany).

Research.

OPENING OF THE MENTAL HEALTH RESEARCH INSTITUTE, VICTORIA.

SIR IAN CLUNIES-ROSS, Director of the Commonwealth Scientific and Industrial Research Organization, opened the Mental Health Research Institute at Royal Park, Melbourne, on May 10, 1956.

Housed in a new building, it is part of the development programme of the Mental Hygiene Authority. The Institute is under the direction of the Chief Clinical Officer of the Mental Hygiene Department, Dr. Alan Stoller.

The Institute is intended to act as a focus for research into mental illness in Victoria; to study and develop aspects of the prevention of mental ill health in Victoria; and to promote community understanding of mental health problems in that State. To this end, it contains a large and increasing mental health library, a board room for group discussions, a teaching unit which includes one-way screen, and offices for research workers. The staff appointed so far includes a research psychologist, a biostatistical research officer, and a mental health education officer. The unit is not intended at present to be a self-contained research centre, but will aim to stimulate and assist personnel within the Mental Hygiene Department, as well as those of other scientific establishments in Victoria, to investigate mental health problems. Pamphlets are being collected, films are being catalogued, and such other material is being obtained as will help professional workers in the community towards gaining better understanding of mental health problems in their work.

Through the Mental Health Research Found, granted annually by the Victorian Government, the Institute is able to cooperate with the University of Melbourne. The Department of Anatomy of the University of Melbourne, at the opening of the Institute, demonstrated its researches into the neuroanatomical bases of emotion and into the growth of mongol children; the Departments of Physiology and Pharmacology displayed some of their work on cerebral sedatives and analeptics; whilst the Department of Pathology gave some indication of its work on cerebral arteriosclerosis. The Mental Hygiene Department, in a group of demonstrations, showed its present wide interest in both the physical and social sciences. The displays showed investigations of the following: the incidence of schizophrenia, Huntington's chorea and juvenile delinquency; the clinical effects of tranquillizing drugs; electroencephalographic studies of brain-damaged children; the results of infero-medial orbital leucotomy; lithium treatment of hyperexcitable states. Also displayed was a study of remedial reading as therapy for emotionally disturbed, educationally backward children.

The Royal Australasian College of Physicians.

ADMISSION OF MEMBERS: AUSTRALIA.

AT a meeting of the Council of The Royal Australasian College of Physicians held in Sydney on June 15, 1956, the following candidates, who were successful at an examination held by the Australian Board of Censors, were admitted to membership of the College: Dr. W. J. Hickey and Dr. I. J. McKelvie, of Queensland; Dr. P. N. Francis, Dr. J. E. Hassall, Dr. W. B. Hennessy, Dr. J. W. Lance, Dr. P. J. Maloney and

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 9, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	6	1(1)	2(1)	..	..	..	..	..	9
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1(1)	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	10(9)	5(4)	3(2)	..	1(1)	..	..	..	19
Diphtheria	..	3(3)	..	..	6(6)	..	..	..	9
Dysentery (Bacillary)	..	3(3)	2(2)	..	1(1)	..	..	..	6
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	58(30)	53(35)	..	3(1)	..	11(4)	2	..	127
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	1	..	..	..	1
Leptospirosis	6	..	2(1)	..	..	..	..	..	8
Malaria	..	1(1)	1	..	..	..	11	..	13
Meningococcal Infection	2	3(1)	..	..	..	..	..	..	5
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	3(1)	9(5)	..	..	1	1(1)	..	1	15
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	3(2)	..	..	1(1)	..	..	..	4
Salmonella Infection	..	..	..	..	3(3)	..	..	..	3
Scarlet Fever	10(5)	13(5)	3	6(5)	..	..	..	..	32
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	39(32)	27(18)	11(4)	8(7)	9(5)	..	2	..	96
Typhoid Fever	..	1	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Dr. B. J. Smith, of New South Wales; Dr. J. M. Bradley and Dr. R. E. Seal, of Victoria; Dr. M. D. Begley and Dr. H. Lander, of South Australia; Dr. J. B. Stokes, of Western Australia.

EXAMINATION FOR MEMBERSHIP.

THE next examination for membership of The Royal Australasian College of Physicians will be held on the following dates: written examination (capital cities), Friday, August 24, 1956; clinical examination (Melbourne), commencing on or about Friday, October 5, 1956. Application forms may be obtained from the Honorary Secretary, 145 Macquarie Street, Sydney, and applications should be lodged with the Honorary Secretary not later than Friday, July 27, 1956.

Notice.

THE ROYAL SOCIETY OF NEW SOUTH WALES.

THE general monthly meeting of the Royal Society of New South Wales will be held on Wednesday, July 4, 1956, at 7.45 p.m., at Science House, Gloucester and Essex Streets, Sydney. The evening will be devoted to a symposium on "The Utilization of Radio-Isotopes", and the following addresses will be given: "Isotopes, their Nature, their Production and Measurement", by Dr. J. Green, School of Chemistry, New South Wales University of Technology; "The Application of Radioactive Isotopes in Medicine", by Dr. A. G. Basser, Institute of Medical Research, Royal North Shore Hospital; "Recent Developments on Isotopes in the United Kingdom and the United States of America", by Dr. J. N. Gregory, Australian Atomic Energy Commission. Members of the British Medical Association are invited to be present.

MEDICAL POST-GRADUATE COURSES OF INSTRUCTION FOR DOCTORS.

THE Royal Institute of Public Health and Hygiene conducts recognized courses of instruction (for medical graduates only) for the examinations for the diploma in public health and the diploma in industrial health held by the Conjoint Board of the Royal College of Surgeons of England, and for the examination for the diploma in industrial health of the Society of Apothecaries of London. The next courses will commence on September 28, 1956. Further information, entry forms and prospectuses may be obtained from the Secretary of the Royal Institute of Public Health and Hygiene, 28 Portland Place, London, W.1, or from the Acting Dean at 23 Queen Square, London, W.C.1.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Brennan, Sean Desmond, L.R.C.P., L.R.C.S. (Dublin), 1949, Main Road, Scarborough, New South Wales.

Clifford, Arnold, M.B., B.S., 1955 (Univ. Sydney), 17 Surfside Avenue, Clovelly, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Calderbank, John William, M.B., B.S., 1956 (Univ. Sydney); Callachor, Thomas Joseph Eugene, M.B., B.S., 1956 (Univ. Sydney); Cowle, Joffré Bartholomew, M.B., B.S., 1956 (Univ. Sydney); Fogland, William Gilbert, M.B., B.S., 1956 (Univ. Sydney); Gapp, Godfrey Leonard, M.B., B.S., 1956 (Univ. Sydney); Andrews, Bruce Allan, M.B., B.S., 1956 (Univ. Sydney); McClure, Eunice Mary, M.B., B.S., 1956 (Univ. Sydney); Smith, Ronald James, M.B., B.S., 1955 (Univ. Sydney); Powell, Philip Arthur McSharry, M.B., B.S., 1953 (Univ. Sydney); Bromhead, Brian Charles, M.B., B.S., 1953 (Univ. Sydney).

The undermentioned has applied for election as a member of the South Australian Branch of the British Medical Association:

McAuliffe, Rodney Francis, qualified 1956, 546 Port Road, Allenby Gardens, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Leeson, Clifford Alfred, M.B., B.S., 1942 (Univ. Adelaide), M.R.C.P.; Potts, Leo, M.B., B.S., 1954 (Univ. Adelaide).

Deaths.

THE following death has been announced:

ROW.—Edward Reginald Row, on June 13, 1956, at Brisbane.

Diary for the Month.

JULY 3.—New South Wales Branch, B.M.A.: Council Quarterly.
JULY 4.—Western Australian Branch, B.M.A.: Branch Council.
JULY 4.—(or July 18) Victorian Branch, B.M.A.: Clinical Meeting.
JULY 6.—Queensland Branch, B.M.A.: General Meeting.
JULY 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JULY 10.—New South Wales Branch, B.M.A.: Organization and Science Committee.
JULY 13.—Tasmanian Branch, B.M.A.: Council Meeting.
JULY 13.—Queensland Branch, B.M.A.: Council Meeting.
JULY 16.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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PUBLISHED WEEKLY

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THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—43RD YEAR SYDNEY, SATURDAY, JUNE 30, 1956 No. 26

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APPLICATIONS are invited from medical graduates for the above position. Previous experience in hæmatology or pathology would be an advantage. Duties are concerned with hæmatology only. The department is a large one, and is responsible for the hæmatological investigation of both in- and out-patients of the Royal Perth Hospital and subsidiary units. The successful applicant would work under a trained full-time hæmatologist, and assist him in the running of the department. There is opportunity for experience in the recent diagnostic techniques, including radioactive tracer methods, and microbiological serum assays. Appointment for 1 to 2 years. The post is a suitable one for a graduate whose interest lies either in a general pathology training, or further training as a hæmatologist.

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ROYAL SOUTH SYDNEY HOSPITAL, JOYNTON AVENUE, ZETLAND, N.S.W.

HONORARY RELIEVING CLINICAL ASSISTANTS (2).

APPLICATIONS are invited from medical practitioners for the positions of Honorary Relieving Clinical Assistants to the Rheumatic Clinic.

The term of appointment is for a period of 12 months, commencing 1st October, 1956.

Applications to the undersigned not later than 31st July, 1956. (Application forms will be forwarded on request.)—R. T. WRIGHT, Secretary and Chief Executive Officer.

BOX HILL AND DISTRICT HOSPITAL, VICTORIA.

HONORARY MEDICAL STAFF.

APPLICATIONS are invited from legally qualified medical practitioners for appointment as Neonatal Pædiatrician and will be received by the undersigned on or before 14th July, 1956. Applicants should possess a relevant senior qualification. Further particulars of the appointment may be obtained by ringing the Medical Superintendent, Dr. R. Kelly, WX 3311. Application forms are available on request.—A. J. ANDREWARTHA, Manager.

JUNIOR PARTNERSHIP OFFERED, western suburbs, Sydney. Residence available for purchase. Goodwill £2000. Terms and finance can be arranged. Reply No. 577, c.o. this office.

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APPLICATIONS are invited for two positions of Resident Medical Officer (Seniors or Juniors) at the Devon Public Hospital (86 General and 22 Midwifery beds).

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Appiy: Surgeon Superintendent, Devon Public Hospital, Latrobe, Tasmania.—E. A. ROGERS, F.C.I.I., L.I.M.A., Secretary.

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS.

WUNDERLY TRAVELLING SCHOLARSHIPS.

APPLICATIONS are invited from legally qualified medical practitioners both in Australia and New Zealand for the award of two Wunderly Travelling Scholarships for 1957. The object of the scholarships is the post-graduate education and training abroad in the diagnosis and management of thoracic disease, of young physicians who may not otherwise have the opportunity of proceeding overseas for such training. The value of the scholarship is one thousand pounds Australian currency (£A.1000) if a scholar is unmarried and one thousand five hundred pounds (£A.1500) if a scholar is married. The scholarship will be tenable by a graduate in medicine of a university approved by the College, who holds a Doctorate of Medicine and/or a Fellowship or Membership of The Royal Australasian College of Physicians or of the Royal College of Physicians of London, but the holding of a higher degree or diploma is not an absolute condition of the award.

The full conditions of award may be obtained from the undersigned. Applications for the 1957 scholarships should reach the undersigned not later than Tuesday, 31 July, 1956.

The successful applicants will be expected to commence their work overseas not later than the beginning of March, 1957.—H. MAYNARD RENNIE, Honorary Secretary.

ALFRED HOSPITAL, COMMERCIAL ROAD, PRAHRAN, VICTORIA.

APPLICATIONS are invited from duly qualified medical practitioners and will be received by the undersigned until 18th July, 1956, for the following appointments:

Tenure of Appointment: Five Years, with Duties to Commence Forthwith.

One Honorary Surgeon to Out-Patients.

Two Honorary Orthopædic Surgeons.

One Honorary Ophthalmic Surgeon.

One Honorary Surgeon for Diseases of Ear, Nose and Throat.

The above appointments have become vacant by reason of retirement and/or resignation of present appointees.

Applications must be submitted on the prescribed form obtainable at the hospital.

Personal canvass will disqualify.—C. G. RANKIN, Manager, 15.6.56.

THE ROYAL WOMEN'S HOSPITAL, MELBOURNE.

HONORARY ASSOCIATE SURGEONS.

APPLICATIONS are invited from duly qualified medical practitioners for the above-mentioned positions.

Eight appointments may be made, *i.e.*, four each to the obstetrical and gynæcological departments, but applicants may apply to work in both departments concurrently.

Further particulars may be obtained from the Medical Superintendent, Dr. J. C. Laver. This advertisement supercedes previous advertisements on the matter.

Applications on the official form close with the undersigned on 9th July, 1956.—A. J. CUNNINGHAM, Manager and Secretary.

THE VICTORIAN EYE AND EAR HOSPITAL, EAST MELBOURNE, VICTORIA.

APPLICATIONS are invited for Resident Medical Officers in the E.N.T. Department of the above hospital, to take up duties as soon as possible.

Salary at the rate of £1125 per annum.

Applicants should have two years' general clinical experience. Previous training in oto-rhino-laryngology is not essential, but preference will be given to those persons intending to take the D.L.O. and who will be prepared to spend up to 18 months at this hospital.

Further particulars and application forms are available from the Medical Superintendent (DR. K. G. HOWSAM).

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(*c*) date of proposed commencement.

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ASSISTANT WANTED by principal of old-established practice, mid-north coast of N.S.W. Rent-free house furnished with essentials. Very little travelling. Oil and benzine supplied. Salary at rate of £2000 per annum. Applicant should have had some surgical experience. Protestant preferred, State age and experience. Reply No. 565, c.o. this office.

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Assistant or partner with view to succession required for large practice in country town with excellent hospital and diagnostic facilities. Preference given to married man with post-graduate surgical and obstetrical experience. Salary £2500 p.a. plus car allowance and percentage according to experience. Furnished house provided. Gross income £15,000. Practice for sale or lease. For further particulars apply HANCOCK AND ROBERTSON, Medical Agents, 205 St. George's Terrace, Perth.

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Further particulars of the appointments may be obtained by ringing the Medical Superintendent, Dr. R. Kelly.

Application forms are available on request.—A. J. ANDREWARTHA, Manager.

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Apply D. MCINNES, Secretary-Manager.

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APPLICATIONS are invited from appropriately qualified medical officers for positions at the above hospital. The salary is: 1st year after graduation £725 p.a., 2nd year after graduation £875 p.a., 3rd year after graduation £1125 p.a., 4th year after graduation £1400 p.a.

Applications will be received by the undersigned on or before 7th July, 1956.

For further information contact the Medical Superintendent, Dr. R. Kelly, WX 3311. — A. J. ANDREWARTHA, Manager.

FOR SALE OR LEASE, unopposed N.S.W. Hunter Valley practice. G.T. £6500. Well-equipped hospital. Lease small percent. Sale £3000 goodwill. Terms without interest or deposit. Reply No. 448, c.o. this office.

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ERIATRICIAN: GREENVALE VILLAGE FOR THE AGED, GREENVALE, VICTORIA.

APPLICATIONS are invited m senior medical officers regis- ed in Victoria for the appoint- nt as Geriatrician at Greenvale llage. This will be a full-time pointment, and salary will be thin the range of £2500-£3250 r annum on appointment, plus arters.

The successful applicant will be commended for the "Sir Edward lstrom and Sir Herbert Olney holarship" of £2000 to enable him study geriatrics abroad for a riod of nine to fifteen months.

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Diploma in Anæsthetics; Diploma in Psychological Medicine; Diploma in Ophthalmology; Diploma in Radiology; Diploma in Laryngology; Diploma in Child Health; F.R.C.S.Eng., and all Surgical Examinations; M.R.C.P.Lond., and all Medical Examinations; M.D. Thesis of all Universities; Courses for all Qualifying Examinations. Complete Guide to Medical Examinations sent free on application. Applicants should state in which qualification they are interested. Address: Secretary, Medical Correspondence College, 19 Welbeck St., London, W.1.

AUCKLAND UNIVERSITY COLLEGE (University of New Zealand).

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APPLICATIONS are invited from qualified persons, preferably, but not necessarily, with medical degrees, for the Sandoz Research Fellowship, Post-Graduate School of Obstetrics and Gynæcology. The person appointed will have the opportunity of participating in existing research projects and to undertake new work as may be agreed upon.

The Fellowship may be held either on a full-time or part-time basis, with preference given to the former.

Salary up to £(N.Z.)1500, according to qualifications and experience.

Further information is available from the undersigned, or from Australian universities, with whom applications will close on the 31st July, 1956.—J. A. KIRKNESS, Registrar.

NEPEAN DISTRICT HOSPITAL, PENRITH, N.S.W.

HONORARY RADIOLOGIST.

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Resident Medical Officer required for six months from 1st July, 1956. Possibility of re-appointment at the end of six months' satisfactory service.

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Further particulars of the appointment may be obtained by ringing the Medical Superintendent, Dr. R. Kelly, WX 3311. Application forms are available on request. —A. J. ANDREWARTHA, Manager.

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The Directors of the Australasian Medical Publishing Company, Limited, wish to appoint an Assistant Editor to THE MEDICAL JOURNAL OF AUSTRALIA. The present editorial staff consists of the Editor, a Deputy Editor, and a Lay Sub-Editor.

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